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=> fil reg
FILE 'REGISTRY' ENTERED AT 13:50:22 ON 05 SEP 2004
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:     3 SEP 2004  HIGHEST RN 739335-06-9
DICTIONARY FILE UPDATES:    3 SEP 2004  HIGHEST RN 739335-06-9

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> d sta que l18
L16              STR
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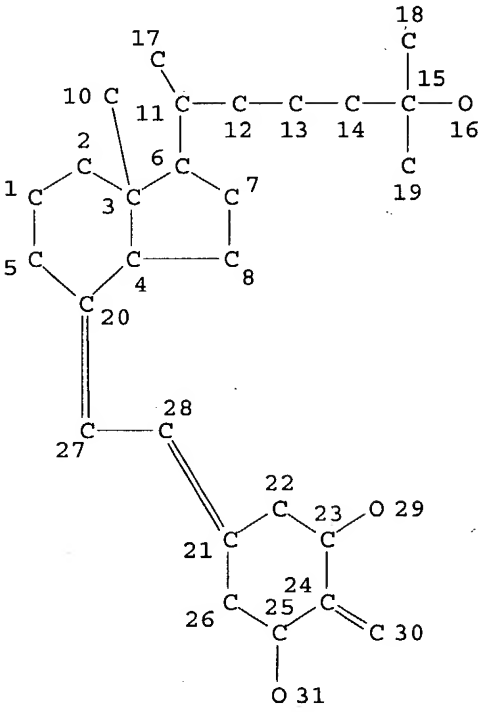

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NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  30

STEREO ATTRIBUTES: NONE
L18            3 SEA FILE=REGISTRY FAM FUL L16
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100.0% PROCESSED 15 ITERATIONS 3 ANSWERS
SEARCH TIME: 00.00.01

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L1            22 S E3,E4,E6,E7
                E CLAGETTE M/AU
L2             1 S E2
                E CLAGETTE D/AU
                E DAME M/AU
L3            12 S E3,E4,E6-E8
                E DELUCA H/AU
L4          1160 S E3,E6-E10
                E DE LUCA H/AU
L5            38 S E5,E6
L6          1213 S L1-L5

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                SET SMARTSELECT OFF

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L9           729 S L8 AND C6/ES AND C5-C6/ES AND 3/NR
L10          294 S L9 AND 3/O
L11           92 S L10 AND 27/C
L12           54 S L11 AND 44/H
L13           23 S L12 AND 1 3 25 TRIOL
L14            2 S L13 AND 2 METHYLENE
L15           52 S L12 NOT L14
L16               STR
L17            0 S L16 FAM SAM
L18            3 S L16 FAM FUL
                SAV L18 QAZI782/A
L19            3 S L14,L18

     FILE 'HCAOLD' ENTERED AT 13:48:18 ON 05 SEP 2004
L20            0 S L18

     FILE 'HCAPLUS' ENTERED AT 13:48:23 ON 05 SEP 2004
L21           22 S L18
L22           19 S L21 AND L6
L23            3 S L21 NOT L22
L24           22 S L21-L23
L25            0 S L24 AND LIFE(L)EXPECT?
L26            0 S L24 AND LONGEV?
                E LONGEVITY/CT
                E E3+ALL
L27            1 S L24 AND E3+OLD,NT,PFT,RT
L28           22 S L24,L27

     FILE 'USPATFULL, USPAT2' ENTERED AT 13:50:06 ON 05 SEP 2004
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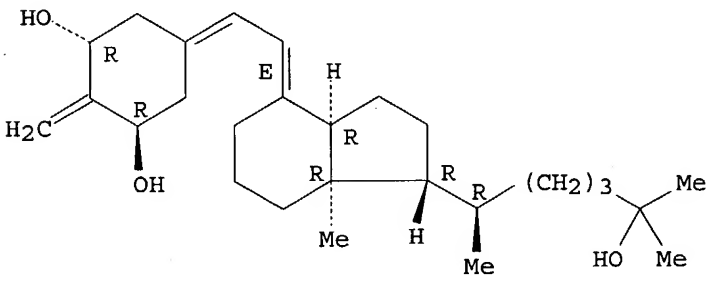
L29 24 S L18

FILE 'REGISTRY' ENTERED AT 13:50:22 ON 05 SEP 2004

=> d ide can tot l18

L18 ANSWER 1 OF 3 REGISTRY COPYRIGHT 2004 ACS on STN
RN 235108-14-2 REGISTRY
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,14β)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C27 H44 O3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.
Double bond geometry as shown.



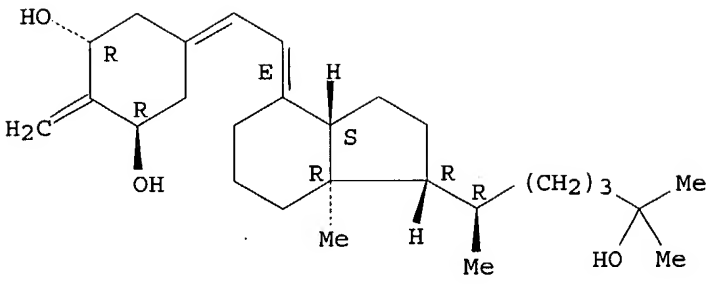
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:144749

L18 ANSWER 2 OF 3 REGISTRY COPYRIGHT 2004 ACS on STN
RN 213319-29-0 REGISTRY
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-1-[(1R)-5-hydroxy-1,5-dimethylhexyl]-7a-methyl-4H-inden-4-ylidene]ethylidene]-, (1R,3R)-
FS STEREOSEARCH
MF C27 H44 O3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); RACT (Reactant or reagent)

Absolute stereochemistry.
Double bond geometry as shown.



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11 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:247113

REFERENCE 2: 139:271426

REFERENCE 3: 136:401925

REFERENCE 4: 136:112696

REFERENCE 5: 135:358086

REFERENCE 6: 135:304063

REFERENCE 7: 135:288953

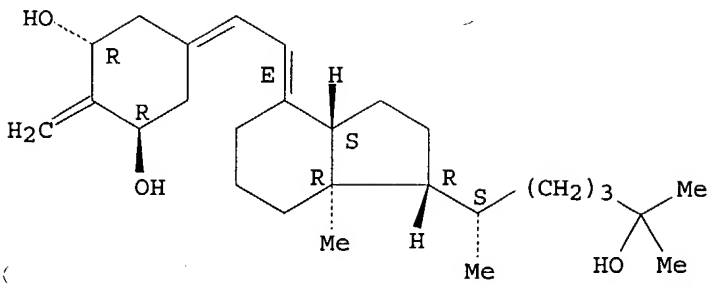
REFERENCE 8: 133:267021

REFERENCE 9: 130:52625

REFERENCE 10: 129:245332

L18 ANSWER 3 OF 3 REGISTRY COPYRIGHT 2004 ACS on STN
RN 213250-70-5 REGISTRY
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-1-[(1S)-5-hydroxy-1,5-dimethylhexyl]-7a-methyl-4H-inden-4-ylidene]ethylidene]-, (1R,3R)-
FS STEREOSEARCH
MF C27 H44 O3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

15 REFERENCES IN FILE CA (1907 TO DATE)
19 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:386155

REFERENCE 2: 140:13126

REFERENCE 3: 139:317525

REFERENCE 4: 139:271459

REFERENCE 5: 138:50247

REFERENCE 6: 136:401925

REFERENCE 7: 136:335278

REFERENCE 8: 136:112696

REFERENCE 9: 135:358086

REFERENCE 10: 135:304063

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 13:50:36 ON 05 SEP 2004
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FILE COVERS 1907 - 5 Sep 2004 VOL 141 ISS 11
FILE LAST UPDATED: 3 Sep 2004 (20040903/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all hitstr l27

L27 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:71881 HCAPLUS
DN 136:112696
ED Entered STN: 25 Jan 2002
TI Use of 2-methylene-19-nor-20(S)-1α,25-dihydroxyvitamin D3 to increase bone strength and for the treatment of skin disease, cancer, and bone disease
IN **Deluca, Hector F.**; Smith, Connie M.
PA Wisconsin Alumni Research Foundation, USA
SO PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-59
CC 1-12 (Pharmacology)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002005823	A2	20020124	WO 2001-US21706	20010710
	WO 2002005823	A3	20020523		
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1301189	A2	20030416	EP 2001-957115	20010710
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	BR 2001012454	A	20030729	BR 2001-12454	20010710
	JP 2004505022	T2	20040219	JP 2002-511755	20010710
	US 2004068129	A1	20040408	US 2003-673629	20030929
PRAI	US 2000-616164	A	20000714		
	WO 2001-US21706	W	20010710		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2002005823	ICM	A61K031-59
JP 2004505022	FTERM	4C086/AA01; 4C086/AA02; 4C086/DA16; 4C086/GA16; 4C086/MA01; 4C086/MA04; 4C086/NA14; 4C086/ZA89; 4C086/ZA96; 4C086/ZA97; 4C086/ZB26
US 2004068129	ECLA	A61K007/48C4D

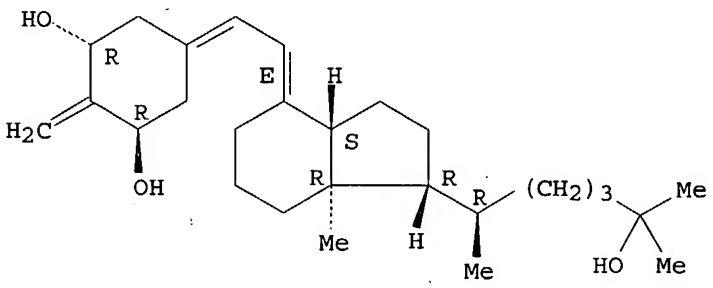
AB The invention provides pharmaceutical uses for 2-methylene-19-nor-20(S)-1α,25-dihydroxyvitamin D3. This compound is characterized by high bone calcium mobilization activity demonstrating preferential activity on bone. This results in a novel therapeutic agent for the treatment of diseases where bone formation is desired, particularly osteoporosis. This compound also exhibits pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte, thus evidencing use as an anticancer agent and for the treatment of skin diseases such as psoriasis. This compound also increases both breaking strength and crushing strength of bones evidencing use in conjunction with bone replacement surgery such as hip and knee replacements.

ST methylenenordihydroxyvitamin D3 bone strength; cancer psoriasis bone disease methylenenordihydroxyvitamin D3; skin disease osteoporosis methylenenordihydroxyvitamin D3; hip knee replacement methylenenordihydroxyvitamin D3

IT Animal cell line
(HL-60; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
IT Mineral elements, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(bone; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
IT Biological transport
(calcium; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
IT Intestine, neoplasm
(colon, inhibitors; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
IT Antitumor agents
(colon; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
IT Cell differentiation
(inducers; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
IT Antitumor agents
(leukemia; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
IT Osteoporosis
(low bone turnover osteoporosis; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
IT Antitumor agents
(mammary gland; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
IT Monocyte
Osteomalacia
Psoriasis
(methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
IT Vitamin D receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
IT Bone
(minerals; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
IT Mammary gland
Prostate gland
(neoplasm, inhibitors; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
IT Drug delivery systems
(oral; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
IT Bone, disease
(osteopenia; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
IT Drug delivery systems
(parenterals; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
IT Osteoporosis
(postmenopausal; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
IT Myelocyte
(promyelocyte; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
IT Antitumor agents
(prostate gland; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)

IT Bone, disease
(renal osteodystrophy; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
IT **Aging, animal**
(senile osteoporosis; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
IT Steroids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(steroid-induced osteoporosis; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
IT Bone
(strength; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
IT Osteoporosis
(therapeutic agents; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
IT Drug delivery systems
(topical; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
IT Drug delivery systems
(transdermal; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
IT 32222-06-3, 1α,25-Dihydroxyvitamin D3 **213319-29-0**
RL: PAC (Pharmacological activity); BIOL (Biological study)
(methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
IT **213250-70-5**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
IT 7440-70-2, Calcium, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(transport; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
IT **213319-29-0**
RL: PAC (Pharmacological activity); BIOL (Biological study)
(methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
RN 213319-29-0 HCAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

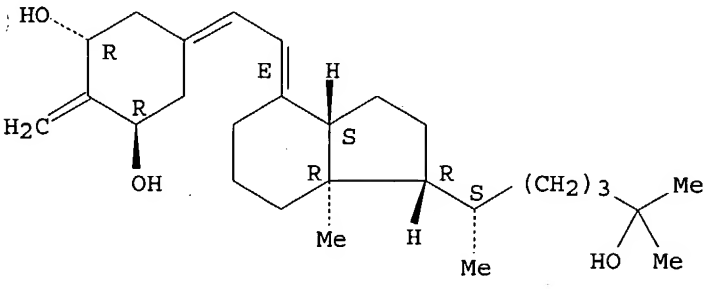
Absolute stereochemistry.
Double bond geometry as shown.



IT **213250-70-5**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methylenenordihydroxyvitamin D3 to increase bone strength and for

treatment of skin disease, cancer, and bone disease)
RN 213250-70-5 HCAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



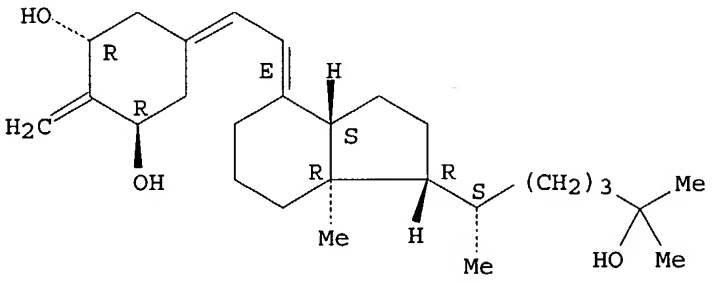
=> s l28 not l27
L30 21 L28 NOT L27

=> d bib abs hitstr retable tot

L30 ANSWER 1 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:522177 HCAPLUS
TI Model of three-dimensional structure of VDR bound with Vitamin D3 analogs substituted at carbon-2
AU Sicinska, Wanda; Rotkiewicz, Piotr; **DeLuca, Hector F.**
CS Department of Biochemistry, University of Wisconsin-Madison, Madison, WI, 53706, USA
SO Journal of Steroid Biochemistry and Molecular Biology (2004), 89-90(1-5), 107-110
CODEN: JSBBEZ; ISSN: 0960-0760
PB : Elsevier Science Ltd.
DT Journal
LA English
AB All Vitamin D analogs possessing the A ring modified at C-2 and showing calcemic activities nest themselves in the VDR binding pocket, oriented towards Tyr 143. Such topol. resembles the position of the Vitamin D hormone in hVDRmt [Proc. Natl. Acad. Sci. U.S.A. 98 (2001) 5491]. Conversely, inactive 2β-methyl-19-nor-analogs anchor the receptor cavity in a distinguishably different manner, namely by their side chain. Moreover, these inactive vitamins have a different conformation around C(6)-C(7) bond. Topol. of modeled complexes suggests that a Vitamin D analog will be biol. active if its intercyclic 5,7-diene moiety assumes parallel position to tryptophan aromatic rings; such orientation allows for creating π-π interactions. The broad comparison of calcemic activities of the analogs, and their interactions with VDR, revealed that specific hydrophobic contacts are involved in bone calcium mobilization (BCM). These contacts occur between 21-Me group and a few amino acids (V296, L305 and L309), conserved in the nuclear receptor superfamily. In the inactive 2β-methyl-19-nor analogs such contacts do not exist. We speculate that two hydrophobic receptor patches, being in close contact with ligand Me groups, might influence interaction with co-modulators involved in calcium homeostasis.
IT **213250-70-5 213319-29-0**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(model of three-dimensional structure of VDR bound with Vitamin D3

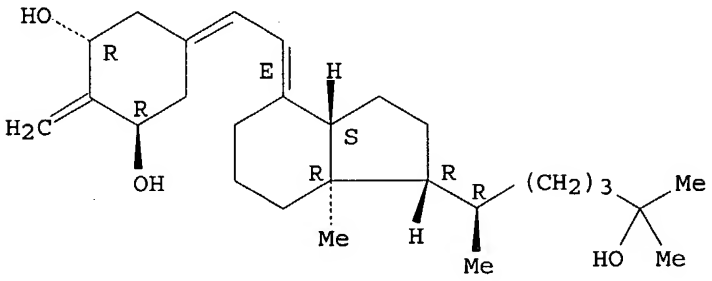
analogs substituted at carbon-2)
RN 213250-70-5 HCAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 213319-29-0 HCAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



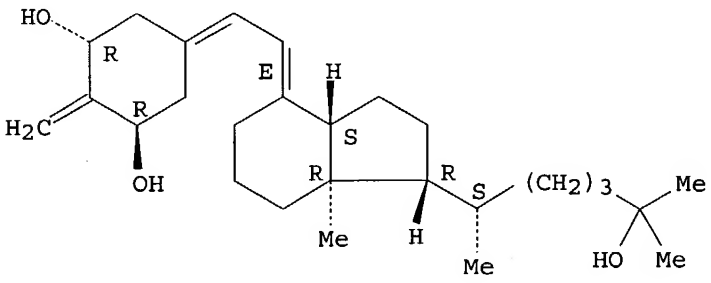
RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
DeLuca, H	1998			US 5847173	HCAPLUS
DeLuca, H	2002			US 6440953	HCAPLUS
Maenpaa, P	2001	66	223	Steroids	HCAPLUS
Okano, T	1989	163	1444	Biochem Biophys Res	HCAPLUS
Pathrose, P	2002	17	2196	J Bone Miner Res	HCAPLUS
Rotkiewicz, P	2001	44	188	Proteins	HCAPLUS
Sicinska, W				unpublished results	
Sicinski, R	1998	41	4662	J Med Chem	HCAPLUS
Sicinski, R	2002	45	3366	J Med Chem	HCAPLUS
Tocchini-Valentini, G	2001	98	5491	Proc Natl Acad Sci U	HCAPLUS
Tripos Inc				SYBYL Modeling Progr	
Yamada, S	2003	23	89	Med Res Rev	HCAPLUS

L30 ANSWER 2 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:522172 HCAPLUS
TI Two-dimensional alanine scanning mutational analysis of the interaction between the vitamin D receptor and its ligands: studies of A-ring modified 19-norvitamin D analogs
AU Shimizu, Masato; Yamamoto, Keiko; Mihori, Mika; Iwasaki, Yukiko; Morizono, Daisuke; Yamada, Sachiko

CS Institute of Biomaterial and Bioengineering, Tokyo Medical and Dental University, Tokyo, 101-0062, Japan
SO Journal of Steroid Biochemistry and Molecular Biology (2004), 89-90(1-5), 75-81
CODEN: JSBBEZ; ISSN: 0960-0760
PB : Elsevier Science Ltd.
DT Journal
LA English
AB To clarify the structure-function relationship (SFR) of vitamin D analogs in terms of their interaction with the vitamin D receptor (VDR), we have proposed a new approach, two-dimensional alanine scanning mutational anal. (2D-ASMA). In this paper, attention was focused on the interactions around the A-ring of vitamin D. For this purpose, we synthesized four new 2-substituted 19-norvitamin D derivs. (3-6). The VDR affinity (3-6: 1, 5, 2 and 1/140, resp.) and transcriptional activity (3-6: 10, 30, 2 and 0.3, resp.) of the four compds. were evaluated relative to 1,25-(OH)2D3 (5) (normalized to 1). Then, the transcriptional activities of wild-type and 18 mutant VDRs induced by the four compds. (3-6) were investigated. The results of this 18+4 2D-ASMA were presented as a patch table, and the effects of the mutations were analyzed in comparison with the natural hormone (1) and 2-methylene-19-nor-20-epi-1,25-(OH)2D3 (2MD, 2). Of the four A-ring analogs, the 2α-hydroxyethoxy derivative (3) showed striking differences in the pattern on the patch table. From the results, we suggest a docking mode of this compound (3) in which the A-ring adopts the α conformation.
IT **213250-70-5**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(two-dimensional alanine scanning mutational anal. of interaction between vitamin D receptor and A-ring modified 19-norvitamin D analogs)
RN 213250-70-5 HCAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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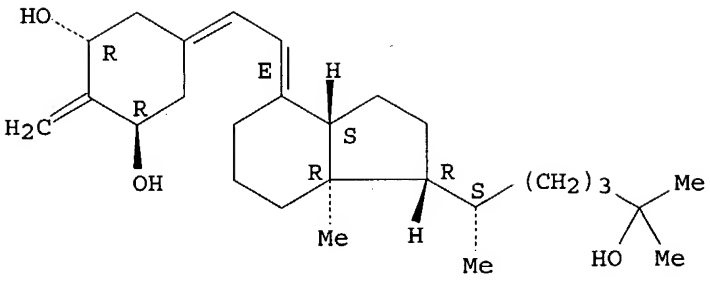
Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Choi, M	2001	9	1721	Bioorg Med Chem	HCAPLUS
Choi, M	2003	10	261	Chem Biol	HCAPLUS
DeLuca, H	1990	8	1	J Bone Miner Metab	
Evans, R	1988	240	889	Science	HCAPLUS
Mangelsdorf, D	1995	83	835	Cell	HCAPLUS
Perlman, K	1991	32	7663	Tetrahedron Lett	HCAPLUS
Pike, J	1997		105	Vitamin D	HCAPLUS
Rochel, N	2001	268	971	Eur J Biochem	HCAPLUS
Rochel, N	2000	5	173	Mol Cell	HCAPLUS
Shevde, N	2002	99	13487	Proc Natl Acad Sci U	HCAPLUS

Shimizu, M	2003	13	809	Bioorg Med Chem Lett	HCAPLUS
Sicinski, R	1998	41	4662	J Med Chem	HCAPLUS
Sicinski, R	2002	45	3366	J Med Chem	HCAPLUS
Tocchini-Valentini, G	2001	98	5491	Proc Natl Acad Sci U	HCAPLUS
Weatherman, R	1999	68	559	Annu Rev Biochem	HCAPLUS
Yamada, S	2000	6	733	Curr Pharm Des	HCAPLUS
Yamada, S	1998	41	1467	J Med Chem	HCAPLUS
Yamada, S	2003	23	89	Med Res Rev	HCAPLUS
Yamamoto, K	1995	5	979	Bioorg Med Chem Lett	HCAPLUS
Yamamoto, K	1999	9	1041	Bioorg Med Chem Lett	HCAPLUS
Yamamoto, K	1996	39	2727	J Med Chem	HCAPLUS
Yamamoto, K	1993	58	2530	J Org Chem	HCAPLUS
Yamamoto, K	2000	97	1467	Proc Natl Acad Sci U	HCAPLUS

L30 ANSWER 3 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:522171 HCAPLUS
TI Therapeutic potential of the 2-alkyl and 2-alkylidene-19-nor-(20S)-modified analogs of 1α,25-dihydroxyvitamin D3
AU **DeLuca, Hector F.**
CS Department of Biochemistry, University of Wisconsin-Madison, Madison, WI, 53706-1544, USA
SO Journal of Steroid Biochemistry and Molecular Biology (2004), 89-90(1-5), 67-73
CODEN: JSBBEZ; ISSN: 0960-0760
PB : Elsevier Science Ltd.
DT Journal
LA English
AB Five analogs of 19-nor-1α,25-dihydroxyvitamin D3 are described that show highly selective and potent activities. The 2-methylene-19-nor-(20S)-1α25-dihydroxyvitamin D3 (2MD) and its 2α-Me sister are selectively active on the osteoblast. 2MD is bone anabolic and causes bone formation in vivo and in vitro and is being developed as a therapy for bone loss diseases such as osteoporosis. 2-Methylene-19-nor (20S)-bishomo-1α-hydroxypregnacalciferol (2BMP) has no activity on calcium in vivo while totally suppressing circulating parathyroid hormone. Its homologs, i.e. 2-methylene-19-nor-1α-hydroxy-homopregnacalciferol (2MP) and 2-methylene-19-nor-1α-hydroxypregnacalciferol (2MPC) act similarly but are either less selective (2MP) or not as potent (2MPC). These abbreviated side chain analogs will be developed for diseases where a rise in serum calcium is not desired, as for example, cancer, renal osteodystrophy, psoriasis and autoimmune diseases.
IT **213250-70-5**
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of 2-alkyl and 2-alkylidene-19-nor-(20S)-modified analogs of 1α,25-(OH)2D3 on PTH activity/bone mineral mobilization, and their therapeutic potential for diseases where a rise in serum calcium is not desired)
RN 213250-70-5 HCAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Abe, J	1990	36	21	J Nutr Sci Vitaminol	HCAPLUS
Binderup, L	1992	3	401	Rev Contemp Pharmaco	
Brown, A	1997		995	Vitamin D	HCAPLUS
Calverley, M	1987	43	4609	Tetrahedron	HCAPLUS
DeLuca, H	1997		3	Vitamin D	HCAPLUS
Jones, G	1998	78	1193	Physiol Rev	HCAPLUS
Jones, G	1997		973	Vitamin D	HCAPLUS
Kobayashi, T	1994	115	373	J Biochem	HCAPLUS
Maung, H	2001	37	532	Am J Kidney Dis	HCAPLUS
Morimoto, S	1989	19	1143	Biochem Int	HCAPLUS
Perlman, K	1990	31	1823	Tetrahedron Lett	HCAPLUS
Plum, L	2002			2-Methyelene-19-nor-	
Shevde, N	2002	99	13487	Proc Natl Acad Sci U	HCAPLUS
Sicinski, R	1998	41	4662	J Med Chem	HCAPLUS
Sicinski, R	2002	45	3366	J Med Chem	HCAPLUS
Slatopolsky, E	1994	5	888	J Am Soc Nephrol	
Slatopolsky, E	2003	85	83	Kidney Int Suppl	
Stabert, B	1989	69	147	Acta Derm Venereol (	
Suda, T	2003	88	259	J Cell Biochem	HCAPLUS
Suda, T	1997		329	Vitamin D	HCAPLUS
Yamamoto, H	2003	278	31756	J Biol Chem	HCAPLUS

L30 ANSWER 4 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:522161 HCAPLUS
TI 2-Methylene analogs of 1α-hydroxy-19-norvitamin D3: synthesis, biological activities and docking to the ligand binding domain of the rat vitamin D receptor
AU Grzywacz, Pawel; **Plum, Lori A.**; Sicinska, Wanda; Sicinski, Rafal R.; Prahl, Jean M.; **DeLuca, Hector F.**
CS Department of Biochemistry, University of Wisconsin-Madison, Madison, WI, 53706, USA
SO Journal of Steroid Biochemistry and Molecular Biology (2004), 89-90(1-5), 13-17
CODEN: JSBBEZ; ISSN: 0960-0760
PB : Elsevier Science Ltd.
DT Journal
LA English
AB In continuing efforts towards the synthesis of biol. active vitamin D compds. of potential therapeutic value, new 2-methylene-1α-hydroxy-19-norvitamin D3 analogs 3 and 4 with modified alkyl side chains have been synthesized. The key synthetic step involved Lythgoe-type Wittig-Horner coupling of Windaus-Grundmann type ketones 9, possessing different 17β-alkyl substituents, with the phosphine oxide 10 prepared from (-)-quinic acid. The prepared vitamins 3 and 4 were .apprx.eight times less potent than 1α,25-dihydroxyvitamin D3 (1α,25-(OH)2D3) (1) in binding to the rat intestinal vitamin D receptor (VDR). In comparison

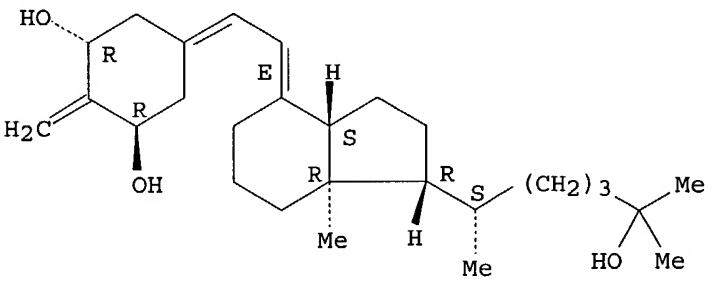
with the hormone 1 they exhibited slightly lower cellular HL-60 differentiation activity. When tested in vivo; the analog 3 was characterized by very high bone calcium mobilizing potency and intestinal calcium transport activity. Unexpectedly, the 25-Me compound 4 showed marked calcemic activity in both assays. Computational docking of the vitamin 3 into the binding pocket of the rat vitamin D receptor is also reported.

IT **213250-70-5P**
RL: BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis, biol. activities of 2-Methylene analogs of 1α-hydroxy-19-norvitamin D3 and their docking to ligand binding domain of rat vitamin D receptor)

RN 213250-70-5 HCAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Dame, M	1986	25	4523	Biochemistry	HCAPLUS
DeLuca, H	1991	3	1129	Comprehensive Medici	
DeLuca, H	1988	2	224	FASEB J	HCAPLUS
Jones, G	1998	78	1193	Physiol Rev	HCAPLUS
Norman, A	1994			Vitamin D, a pluripo	
Ostrem, V	1987	262	14164	J Biol Chem	HCAPLUS
Posner, G	1995	38	4529	J Med Chem	HCAPLUS
Rochel, N	2000	5	173	Mol Cell	HCAPLUS
Rotkiewicz, P	2001	44	188	Proteins	HCAPLUS
Shevde, N	2002	99	13487	Proc Natl Acad Sci U	HCAPLUS
Sicinski, R	1998	41	4662	J Med Chem	HCAPLUS
Suda, T	1990	10	195	Annu Rev Nutr	HCAPLUS

L30 ANSWER 5 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2004:220021 HCAPLUS

DN 140:247113

TI Method of extending the dose range of vitamin D compounds

IN **Deluca, Hector F.**; Pike, John W.; Shevde, Nirupama; **Plum, Lori A.**; Clagett-Dame, Margaret

PA USA

SO U.S. Pat. Appl. Publ., 17 pp.
CODEN: USXXCO

DT Patent

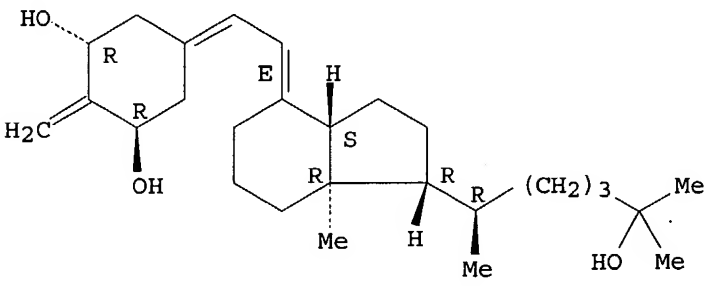
LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI US 2004053813 A1 20040318 US 2002-235244 20020905
WO 2004022068 A1 20040318 WO 2003-US20517 20030626
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRAI US 2002-235244 A 20020905
OS MARPAT 140:247113
AB Inhibitors of bone calcium resorption are administered to allow high doses of vitamin D compds. or mimetics (Markush structures are given) to be given with the intent of treating non-calcium related diseases such as cancer, psoriasis, and autoimmune disease without the dangers of calcification of kidney, heart, and aorta. Inhibitors of bone calcium resorption include the bis-phosphonates, OPG or the soluble RANKL receptor known as sRANK, and function to block the availability of calcium from bone thereby preventing hypercalcemia and the resulting calcification of soft tissues. Thus, high doses of 1α,25-dihydroxyvitamin D 3 (1,25-(OH) 2 D 3), its analogs, prodrugs, or mimetics can be utilized with minimal risk to a patient. Specifically, alendronate is shown to block the bone calcium mobilization activity of both 1,25-(OH) 2 D 3 and its very potent analog, 2-methylene-19-nor-20(S)-1α,25-dihydroxyvitamin D 3 .
IT **213319-29-0**
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method of extending dose range of vitamin D compds.)
RN 213319-29-0 HCAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

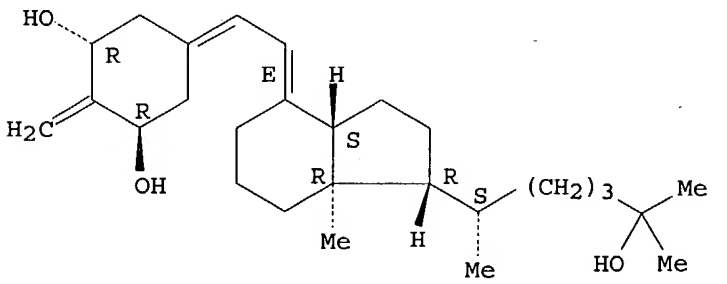
Absolute stereochemistry.
Double bond geometry as shown.



L30 ANSWER 6 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:191311 HCAPLUS
DN 140:386155
TI Molecular structure of rat vitamin D receptor ligand binding domain complexed with 2-carbon-substituted vitamin D3 hormone analogs and a LXXLL-containing coactivator peptide
AU Vanhooke, Janeen L.; Benning, Matthew M.; Bauer, Cary B.; Pike, J. Wesley; **DeLuca, Hector F.**
CS Department of Biochemistry, University of Wisconsin, Madison, WI, 53706, USA

SO Biochemistry (2004), 43(14), 4101-4110
CODEN: BICHAW; ISSN: 0006-2960
PB American Chemical Society
DT Journal
LA English
AB The authors have determined the crystal structures of the ligand binding domain (LBD) of the rat vitamin D receptor in ternary complexes with a synthetic LXXLL-containing peptide and the following four ligands: 1α,25-dihydroxyvitamin D3; 2-methylene-19-nor-(20S)-1α,25-dihydroxyvitamin D3 (2MD); 1α-hydroxy-2-methylene-19-nor-(20S)-bishomopregnacalciferol (2MbisP), and 2α-methyl-19-nor-1α,25-dihydroxyvitamin D3 (2AM20R). The conformation of the LBD is identical in each complex. Binding of the 2-carbon-modified analogs does not change the positions of the amino acids in the ligand binding site and has no effect on the interactions in the coactivator binding pocket. The CD ring of the superpotent analog, 2MD, is tilted within the binding site relative to the other ligands in this study and to (20S)-1α,25-dihydroxyvitamin D3. The aliphatic side chain of 2MD follows a different path within the binding site; nevertheless, the 25-hydroxyl group at the end of the chain occupies the same position as that of the natural ligand, and the hydrogen bonds with histidines 301 and 393 are maintained. 2MbisP binds to the receptor despite the absence of the 25-hydroxyl group. A water mol. is observed between His 301 and His 393 in this structure, and it preserves the orientation of the histidines in the binding site. Although the α-chair conformer is highly favored in solution for the A ring of 2AM20R, the crystal structures demonstrate that this ring assumes the β-chair conformation in all cases, and the 1α-hydroxyl group is equatorial. The peptide folds as a helix and is anchored through hydrogen bonds to a surface groove formed by helixes 3, 4, and 12. Electrostatic and hydrophobic interactions between the peptide and the LBD stabilize the active receptor conformation. This stabilization appears necessary for crystal growth.
IT **213250-70-5**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(mol. structure of rat vitamin D receptor ligand binding domain complexed with 2-carbon-substituted vitamin D3 hormone analogs and LXXLL-containing coactivator peptide)
RN 213250-70-5 HCAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Abe, E	1981	78	4990	Proc Natl Acad Sci U	HCAPLUS
Binderup, L	1991	42	1569	Biochem Pharmacol	HCAPLUS

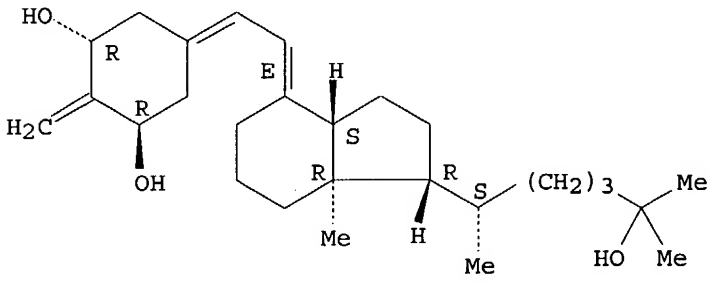
Bortman, P	2002	35	1	Braz J Med Biol Res	HCAPLUS
Bouillon, R	1995	16	200	Endocr Rev	HCAPLUS
Bourguet, W	1995	375	377	Nature	HCAPLUS
Chothia, C	1975	254	304	Nature	HCAPLUS
Collaborative Computati	1994	50	760	Acta Crystallogr, Se	
Dame, M	1985	82	7825	Proc Natl Acad Sci U	HCAPLUS
Darimont, B	1998	12	3343	Genes Dev	HCAPLUS
Delano, W	2002			The PyMOL molecular	
Drezner, M	1997		733	Vitamin D	HCAPLUS
Durand, B	1994	13	5370	EMBO J	HCAPLUS
Fraser, D	1973	289	817	N Engl J Med	MEDLINE
Glorieux, F	1980	303	1023	N Engl J Med	MEDLINE
Hayes, C	2000	59	531	Proc Nutr Soc	HCAPLUS
Henttu, P	1997	17	1832	Mol Cell Biol	HCAPLUS
Hosomi, J	1983	113	1950	Endocrinology	HCAPLUS
Ikekawa, N	1987	7	333	Med Res Rev	HCAPLUS
Jones, G	1998	78	1193	Physiol Rev	HCAPLUS
Kabsch, W	1976	32	922	Acta Crystallogr, Se	
Kimmel-Jehan, C	1997	341	75	Arch Biochem Biophys	HCAPLUS
Konety, B	2002	29	95	Urol Clin North Am	
Lamberg-Allardt, C	1991	49	S46	Calcif Tissue Int	
Langner, A	1993	128	566	Br J Dermatol	MEDLINE
Laskowski, R	1993	26	283	J Appl Crystallogr	HCAPLUS
Lee, B	1971	55	379	J Mol Biol	HCAPLUS
Lemire, J	1992	49	26	J Cell Biochem	HCAPLUS
Macdonald, P	1991	266	18808	J Biol Chem	HCAPLUS
Massry, S	1979	242	1875	JAMA	MEDLINE
Masuyama, H	1997	11	1507	Mol Endocrinol	HCAPLUS
Murshudov, G	1997	53	240	Acta Crystallogr, Se	
Nishii, Y	2001	66	137	Steroids	HCAPLUS
Nolte, R	1998	395	137	Nature	HCAPLUS
Okamura, W	1974	71	4194	Proc Natl Acad Sci U	HCAPLUS
Osborn, J	1995	1	195	Urol Oncol	
Rachez, C	2000	246	9	Gene	HCAPLUS
Rachez, C	2000	20	2718	Mol Cell Biol	HCAPLUS
Renaud, J	1995	378	681	Nature	HCAPLUS
Rochel, N	2000	5	173	Mol Cell	HCAPLUS
Ross, T	1991	88	6555	Proc Natl Acad Sci U	HCAPLUS
Roussel, A	1991		86	Silicone Graphics Ge	
Shevde, N	2002	99	13487	Proc Natl Acad Sci U	HCAPLUS
Sicinski, R	1998	41	4662	J Med Chem	HCAPLUS
Sicinski, R	2002	45	3366	J Med Chem	HCAPLUS
Slatopolski, E	1997		849	Vitamin D	
Smith, E	1986	86	709	J Invest Dermatol	HCAPLUS
Tanaka, H	1982	204	713	Biochem J	HCAPLUS
Tocchini-Valentini, G	2001	98	5491	Proc Natl Acad Sci U	HCAPLUS
Vagin, A	1997	30	1022	J Appl Crystallogr	HCAPLUS
Wing, R	1975	97	4980	J Am Chem Soc	HCAPLUS

L30 ANSWER 7 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:796501 HCAPLUS
DN 139:271459
TI Use of carbon-2-modified-vitamin D analogs to induce the formation of new bone
IN **Deluca, Hector F.**; Pike, J. Wesley; Shevde, Nirupama K.
PA Wisconsin Alumni Research Foundation, USA
SO PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI WO 2003082300 A1 20031009 WO 2003-US7443 20030312
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2003195175 A1 20031016 US 2002-105826 20020325
PRAI US 2002-105826 A 20020325
OS MARPAT 139:271459
AB It has been discovered that the 2-carbon-modified derivs. of 1α,25-dihydroxyvitamin D3 specifically stimulate osteoblasts to form new bone. The ability of the 2-carbon-modified vitamin D analogs to stimulate new bone formation suggest that these compds. can be used where synthesis of new bone is required. Thus, these compds. can be used either systemically or locally to stimulate the growth of bone transplants, to increase the rate of fracture healing and thereby reduce the time required for the healing of fractures, the stimulation of bone growth when required for replacement surgery, and also for the growth of bone to implants or other devices required to maintain the skeleton or teeth in the proper positions.
IT **213250-70-5**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of carbon-2-modified-vitamin D analogs to induce the formation of new bone)
RN 213250-70-5 HCAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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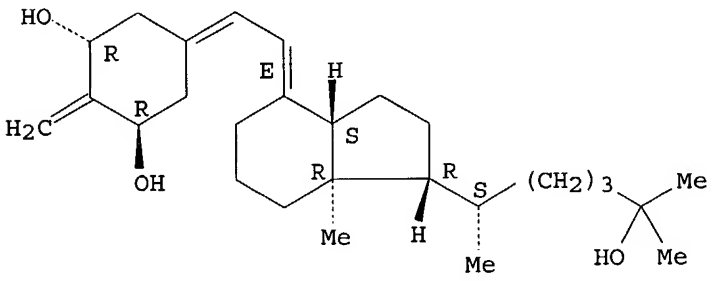
Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Schnoes, H	1997			WO 9711053 A	HCAPLUS
Shevde, N	2002	99	13487	PROCEEDINGS OF THE N	HCAPLUS
Sicinski	1998	41	4662	JOURNAL OF MEDICINAL	HCAPLUS
Wisconsin Alumni Res Fo	1998			WO 9841500 A	HCAPLUS
Wisconsin Alumni Res Fo	1998			WO 9841501 A	HCAPLUS
Wisconsin Alumni Res Fo	2001			WO 0174766 A	HCAPLUS
Wisconsin Alumni Res Fo	2002			WO 0205823 A	HCAPLUS
Wisconsin Alumni Res Fo	2002			WO 0205824 A	

L30 ANSWER 8 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:680362 HCAPLUS
DN 140:13126
TI Vitamin D analogs and calcium metabolism. Bone-selective analogs
AU Okano, Toshio
CS Department of Hygienic Sciences, Kobe Pharmaceutical University, Japan
SO Clinical Calcium (2003), 13(7), 911-914
CODEN: CLCCEJ; ISSN: 0917-5857
PB Iyaku Janarusha
DT Journal; General Review
LA Japanese
AB A review. 2MD [2-methylene-19-nor-(20S)-1α,25(OH)2D3] is a bone-selective vitamin D analog that has been developed on the basis of structure-function study. The bone-selective action of the analog has been tested and confirmed both in vitro and in vivo and its clin. application as a medication for bone diseases is anticipated although its adverse effects remain unclear.
IT **213250-70-5**
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(clin. applications of bone-selective vitamin D analogs and relationship to calcium metabolism)
RN 213250-70-5 HCAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



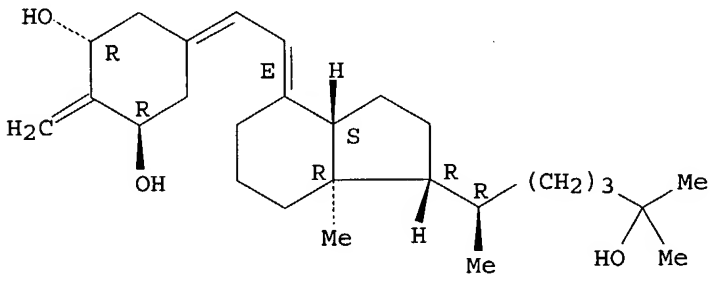
L30 ANSWER 9 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:647469 HCAPLUS
DN 139:271426
TI 2-Methylene-19-nor-(20S)-1,25-dihydroxyvitamin D3 potently stimulates gene-specific DNA binding of vitamin D receptor in osteoblasts
AU Yamamoto, Hironori; Shevde, Nirupama K.; Warrier, Anjali; **Plum, Lori A.**; **DeLuca, Hector F.**; Pike, J. Wesley
CS Department of Biochemistry, University of Wisconsin-Madison, Madison, WI, 53706, USA
SO Journal of Biological Chemistry (2003), 278(34), 31756-31765
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
AB 2-Methylene-19-nor-(20S)-1,25-dihydroxyvitamin D3 (2MD) is a highly potent analog of 1,25-dihydroxyvitamin D3 (1,25(OH)2D3) whose actions are mediated through the vitamin D receptor (VDR). The authors have replicated this increased potency of 2MD in vitro using osteoblastic cells and explored its underlying mol. mechanism. 2MD stimulates the expression of several vitamin D-sensitive genes including 25-hydroxyvitamin D3-24 hydroxylase (Cyp24), osteopontin and receptor activator of NFκB

ligand and suppresses osteoprotegerin at concns. two logs lower than that for 1,25(OH)2D3. 2MD is also more potent in stimulating transfected chimeric reporter genes under either Cyp24 or the osteocalcin promoter control. Enhanced potency is retained regardless of medium serum content. Interestingly, the uptake of both 1,25(OH)2D3 and 2MD into cells is similar, as is their rapid association with the VDR. This indicates that comparable levels of occupied VDR do not elicit equivalent levels of transactivation. Using chromatin immunopptn. (ChIP), however, the authors observed a strong correlation between DNA-bound receptor and the level of induced transcription suggesting a 2MD-induced increase in affinity of the VDR for DNA. Addnl. studies using a mammalian two-hybrid system and ChIP indicate that 2MD is also more potent in promoting interaction with RXR and the coactivators SRC-1 and DRIP205. Finally, protease digestion studies revealed a unique VDR conformation in the presence of 2MD. These studies suggest that the mol. mechanism of 2MD potency is due to its ability to promote enhanced levels of specific DNA binding by the VDR and could suggest possible explanations for the tissue- and gene-selective actions of 2MD.

IT **213319-29-0**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(2-methylene-19-nor-(20S)-1,25-dihydroxyvitamin D3 potently stimulates gene-specific DNA binding of vitamin D receptor in osteoblasts in relation to underlying mol. mechanism)

RN 213319-29-0 HCAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Allan, G	1992	267	19513	J Biol Chem	HCAPLUS
Beckman, M	1998	35	1	Prog Med Chem	HCAPLUS
Beekman, J	1993	7	1266	Mol Endocrinol	HCAPLUS
Bikle, D	1992	13	765	Endocr Rev	HCAPLUS
Binderup, L	1997		1027	Vitamin D	HCAPLUS
Brown, A	1997		1027	Vitamin D	
Carlberg, C	2003	88	274	J Cell Biochem	HCAPLUS
Chang, C	1999	19	8226	Mol Cell Biol	HCAPLUS
Cheskis, B	1996	12	3309	Biochemistry	
Cook, N	1984	10	294	Endocr Rev	
Dwivedi, P	2002	277	29643	J Biol Chem	HCAPLUS
Haussler, M	1998	13	325	J Bone Miner Res	HCAPLUS
Heery, D	1997	387	733	Nature	HCAPLUS
Herdick, M	2000	57	1206	Mol Pharmacol	HCAPLUS
Hofbauer, L	2000	15	2	J Bone Miner Res	HCAPLUS
Hughes, M	1988	242	1702	Science	HCAPLUS
James, A	2002	16	2692	Mol Endocrinol	HCAPLUS

Jin, C	1996	10	945	Mol Endocrinol	HCAPLUS
Jones, G	1998	78	1193	Physiol Rev	HCAPLUS
Kissmeyer, A	1991	41	1601	Biochem Pharmacol	HCAPLUS
Kittaka, A	2003	51	357	Chem Pharm Bull (Tok	HCAPLUS
Kraichely, D	1999	274	14352	J Biol Chem	HCAPLUS
Kubodera, N	2003	88	286	J Cell Biochem	HCAPLUS
Li, Y	1997	94	9831	Proc Natl Acad Sci U	HCAPLUS
Liu, Y	2000	14	1776	Mol Endocrinol	HCAPLUS
Mackey, S	1996	10	298	Mol Endocrinol	HCAPLUS
Masuyama, H	1998	71	429	J Cell Biochem	HCAPLUS
McKenna, N	1999	20	321	Endocr Rev	HCAPLUS
Morony, S	1999	14	1478	J Bone Miner Res	HCAPLUS
Nawaz, Z	1999	96	1858	Proc Natl Acad Sci U	HCAPLUS
Norman, A	1995	22	S218	J Cell Biochem	
Ozono, K	1990	265	21881	J Biol Chem	HCAPLUS
Pathrose, P	2002	17	2196	J Bone Miner Res	HCAPLUS
Peleg, S	1995	270	10551	J Biol Chem	HCAPLUS
Pike, A	2000	28	396	Biochem Soc Trans	HCAPLUS
Pike, J	2002	9	168	Adv Ren Replace Ther	
Pike, J	1983	258	1289	J Biol Chem	HCAPLUS
Pike, J	1983	258	8554	J Biol Chem	HCAPLUS
Rochel, N	2000	5	173	Mol Cell	HCAPLUS
Rowan, B	2000	275	4475	J Biol Chem	HCAPLUS
Shang, Y	2000	103	843	Cell	HCAPLUS
Shevde, N	2000	97	7829	Proc Natl Acad Sci U	HCAPLUS
Shevde, N	2002	99	13487	Proc Natl Acad Sci U	HCAPLUS
Shiau, A	1998	95	927	Cell	HCAPLUS
Sicinski, R	1998	41	4662	J Med Chem	HCAPLUS
Sone, T	1991	266	23296	J Biol Chem	HCAPLUS
Thompson, P	2001	27	211	J Mol Endocrinol	HCAPLUS
Tocchini-Valentini, G	2001	98	5491	Proc Natl Acad Sci U	HCAPLUS
Vaisanen, S	1999	261	706	Eur J Biochem	HCAPLUS
Weinman, A	2002	26	37	Methods	
Yang, W	1999	274	16838	J Biol Chem	HCAPLUS
Zou, A	1997	272	19027	J Biol Chem	HCAPLUS

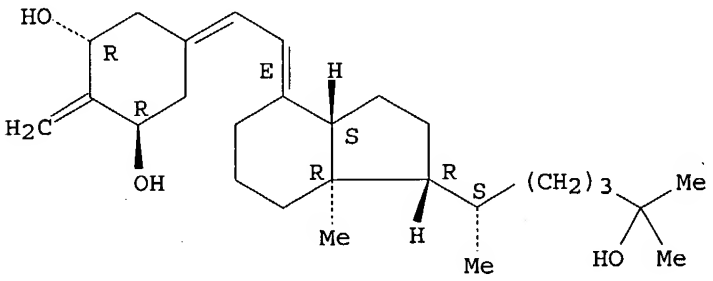
L30 ANSWER 10 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:249861 HCAPLUS
DN 139:317525
TI Interaction between vitamin D receptor and vitamin D ligands two-dimensional alanine scanning mutational analysis
AU Choi, Mihwa; Yamamoto, Keiko; Itoh, Toshimasa; Makishima, Makoto; Mangelsdorf, David J.; Moras, Dino; **DeLuca, Hector F.**; Yamada, Sachiko
CS Institute of Biomaterials and Bioengineering, Tokyo Medical and Dental University, Chiyoda-ku, Tokyo, 101-0062, Japan
SO Chemistry & Biology (2003), 10(3), 261-270
CODEN: CBOLE2; ISSN: 1074-5521
PB Cell Press
DT Journal
LA English
AB We present a new method to investigate the details of interaction between vitamin D nuclear receptor (VDR) and various ligands, namely a two-dimensional alanine scanning mutational anal. In this method, the transactivation of various ligands is studied in conjunction with a series of alanine scanning mutations of the residues lining the ligand binding pocket (LBP) of VDR, and the complete set of results is profiled in a patch table. We investigated examples from four structurally diverse groups of known VDR ligands: the native vitamin D hormone and two compds. with the same side chain configuration; four 20-epi compds.; three 19-nor compds.; and two nonsecosteroids. The patch table of the results indicates characteristics of each group in terms of its interaction with 18 LBP residues. We demonstrate the validity of this approach by

application to docking studies of the two nonsecosteroids.

IT **213250-70-5**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(two-dimensional alanine scanning mutational anal. and modeling of the interaction between vitamin D receptor (VDR) its ligands)

RN 213250-70-5 HCAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



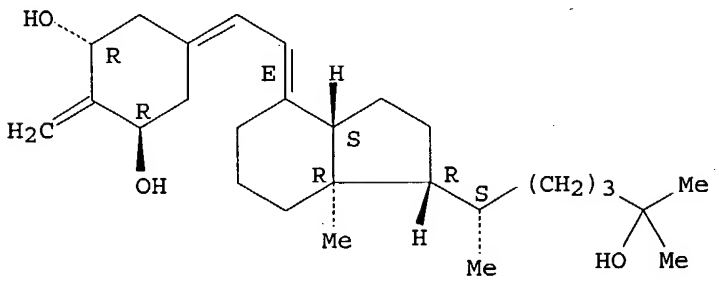
RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Binderup, L	1991	42	1569	Biochem Pharmacol	HCAPLUS
Choi, M	2001	9	1721	Bioorg Med Chem	HCAPLUS
DeLuca, H	1990	8	1	J Bone Miner Metab	
Evans, R	1988	240	889	Science	HCAPLUS
Geller, D	2000	289	119	Science	HCAPLUS
Kobayashi, T	1993	3	1815	Bioorg Med Chem Lett	HCAPLUS
Kragballe, K	1997		1213	Vitamin D	HCAPLUS
Kramer, B	1999	37	228	Proteins	HCAPLUS
Makishima, M	2002	296	1313	Science	HCAPLUS
Mangelsdorf, D	1995	83	835	Cell	HCAPLUS
Murayama, E	1986	34	4410	Chem Pharm Bull (Tok	HCAPLUS
Narisawa, T	1974	53	1093	J Natl Cancer Inst	HCAPLUS
Noda, M	1990	87	9995	Proc Natl Acad Sci U	HCAPLUS
Pike, J	1983	258	1289	J Biol Chem	HCAPLUS
Rarey, M	1996	261	470	J Mol Biol	HCAPLUS
Rochel, N	2001	268	971	Eur J Biochem	HCAPLUS
Rochel, N	2000	5	173	Mol Cell	HCAPLUS
Shevde, N	2002	99	13487	Proc Natl Acad Sci U	HCAPLUS
Sicinski, R	2002			US 6440953	HCAPLUS
Sicinski, R	1998	41	4662	J Med Chem	HCAPLUS
Tocchini-Valentini, G	2001	98	5491	Proc Natl Acad Sci U	HCAPLUS
Umesono, K	1991	65	1255	Cell	HCAPLUS
Watkins, R	2001	292	2329	Science	HCAPLUS
Wurtz, J	1996	3	87	Nat Struct Biol	HCAPLUS
Yamada, S	1998			WO 9839292	HCAPLUS
Yamada, S	2000	6	733	Curr Pharm Des	HCAPLUS
Yamada, S	1998	41	1467	J Med Chem	HCAPLUS
Yamamoto, K	1995	5	979	Bioorg Med Chem Lett	HCAPLUS
Yamamoto, K	1999	9	1041	Bioorg Med Chem Lett	HCAPLUS
Yamamoto, K	1996	39	2727	J Med Chem	HCAPLUS
Yamamoto, K	1993	58	2530	J Org Chem	HCAPLUS
Yamamoto, K	2000	97	1467	Proc Natl Acad Sci U	HCAPLUS

L30 ANSWER 11 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:806513 HCAPLUS

DN 138:50247
TI A potent analog of 1α,25-dihydroxyvitamin D3 selectively induces bone formation
AU Shevde, Nirupama K.; **Plum, Lori A.**; Clagett-Dame, Margaret; Yamamoto, Hironori; Pike, J. Wesley; **DeLuca, Hector F.**
CS Department of Biochemistry, University of Wisconsin, Madison, WI, 53706, USA
SO Proceedings of the National Academy of Sciences of the United States of America (2002), 99(21), 13487-13491
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
AB 1,25-Dihydroxyvitamin D3 [1,25(OH)2D3] is a principal regulator of calcium and phosphorus homeostasis through actions on intestine, kidney, and bone. 1,25(OH)2D3 is not considered to play a significant role in bone formation, except for its role in supporting mineralization. The authors report on the properties of 2-methylene-19-nor-(20S)-1α,25(OH)2D3 (2MD), a highly potent analog of 1,25(OH)2D3 that induces bone formation both in vitro and in vivo. Selectivity for bone was first demonstrated through the observation that 2MD is at least 30-fold more effective than 1,25(OH)2D3 in stimulating osteoblast-mediated bone calcium mobilization while being only slightly more potent in supporting intestinal calcium transport. 2MD is also highly potent in promoting osteoblast-mediated osteoclast formation in vitro, a process essential to both bone resorption and formation. Most significantly, 2MD at concns. as low as 10-12 M causes primary cultures of osteoblasts to produce bone in vitro. This effect is not found with 1,25(OH)2D3 even at 10-8 M, suggesting that 2MD might be osteogenic in vivo. Indeed, 2MD (7 pmol/day) causes a substantial increase (9%) in total body bone mass in ovariectomized rats over a 23-wk period. 1,25(OH)2D3 (500 pmol three times a week) only prevented the bone loss associated with ovariectomy and did not increase bone mass. These results indicate that 2MD is a potent bone-selective analog of 1,25(OH)2D3 potentially effective in treating bone loss diseases.
IT **213250-70-5**
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dihydroxyvitamin D3 analog effects on bone metabolism and induction of bone formation)
RN 213250-70-5 HCAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Blunt, J	1968	61	1503	Proc Natl Acad Sci U	HCAPLUS

Carlsson, A	1952	26	212	Acta Physiol Scand	HCAPLUS
DeLuca, H	1981	75	333	Harvey Lect	HCAPLUS
Denhardt, D	1998	30-31	92	J Cell Biochem	
Kong, Y	1999	397	315	Nature	HCAPLUS
Lamm, M	1958	66	204	Arch Pathol	HCAPLUS
Li, Y	1998	139	4391	Endocrinology	HCAPLUS
Liu, Y	2000	14	1776	Mol Endocrinol	HCAPLUS
Morony, S	1999	14	1478	J Bone Miner Res	HCAPLUS
Orimo, H	1987	3	47	Bone Miner	MEDLINE
Paaren, H	1977		890	J Chem Soc Chem Comm	HCAPLUS
Perlman, K	1990	29	190	Biochemistry	HCAPLUS
Rodan, G	1996		289	Osteoporosis	
Shen, J	2002	277	20284	J Biol Chem	HCAPLUS
Shevde, N	2001	38	606	Cleft Palate Craniof	MEDLINE
Shevde, N	2000	97	7829	Proc Natl Acad Sci U	HCAPLUS
Shipley, P	1925	30	37	Am J Dis Child	
Sicinski, R	1998	41	4662	J Med Chem	HCAPLUS
Simonet, W	1997	89	309	Cell	HCAPLUS
Suda, T	1970	100	1049	J Nutr	HCAPLUS
Takahashi, N	1988	123	2600	Endocrinology	HCAPLUS
Tilyard, M	1992	326	357	N Engl J Med	MEDLINE
Underwood, J	1984	246	E493	Am J Physiol	HCAPLUS
Yang, W	1999	274	16838	J Biol Chem	HCAPLUS
Zierold, C	1994	91	900	Proc Natl Acad Sci U	HCAPLUS

L30 ANSWER 12 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:387626 HCAPLUS
DN 136:401925
TI Preparation of 26,27-homologated-20-epi-2-alkylidene-19-nor-vitamin D compounds as antiosteoporotics and antitumor agents
IN **Deluca, Hector F.**; Sicinski, Rafal R.
PA Wisconsin Alumni Research Foundation, USA
SO U.S., 22 pp., Cont.-in-part of U.S. Ser. No. 370,966, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6392071	B1	20020521	US 2000-540686	20000331
	US 5843928	A	19981201	US 1997-819693	19970317
	US 5936133	A	19990810	US 1998-151113	19980910
	WO 2001074766	A1	20011011	WO 2001-US10317	20010329
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1268416	A1	20030102	EP 2001-920897	20010329
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2003529581	T2	20031007	JP 2001-572461	20010329
	US 2002087015	A1	20020704	US 2001-1711	20011031
	US 6537981	B2	20030325		
	US 2003181427	A1	20030925	US 2003-352745	20030128
	US 6696431	B2	20040224		
	US 2004167104	A1	20040826	US 2004-780103	20040217
PRAI	US 1997-819693	A3	19970317		
	US 1998-151113	A1	19980910		

	US 1999-370966	B2	19990810
	US 2000-540686	A	20000331
	WO 2001-US10317	W	20010329
	US 2001-1711	A3	20011031
	US 2003-352745	A3	20030128

OS MARPAT 136:401925
GI

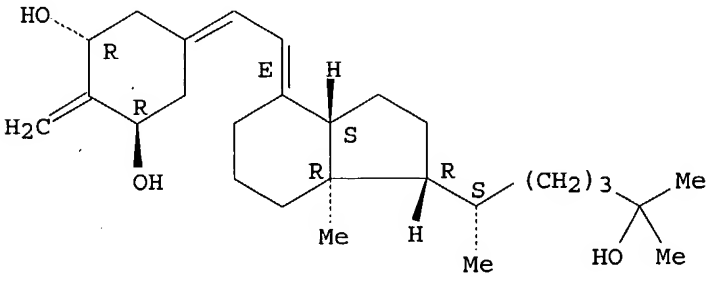
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Novel vitamin D related compds., namely, 2-alkylidene-19-nor-vitamin D derivs. of formula I [Y1, Y2 = H, protecting group; R6, R8 = alkyl, hydroxyalkyl, fluoroalkyl, etc., or when taken together represent the group -(CH2)x- where x is an integer from 2 to 5; R = any of the typical side chains known for vitamin D type compds.] are prepared These 2-substituted compds. are characterized by low intestinal calcium transport activity and high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. Thus, 20(S)-1α,25-dihydroxy-2-methylene-26,27-dihomo-19-nor-vitamin D3 (II) was prepared via a multistep synthetic sequence starting from 20(S)-25-hydroxy Grundmann's ketone analog III and phosphine oxide IV. The intestinal calcium transport and serum calcium (bone calcium mobilization) activities in vitamin D-deficient rats on a low calcium diet responding to chronic doses of II at 15 pmol/day/7 days were 4.0 ± 0.4 S/M and 5.3 ± 0.1 S/M resp. These compds. also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis.

IT **213250-70-5P 213319-29-0P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 26,27-homologated-20-epi-2-alkylidene-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)

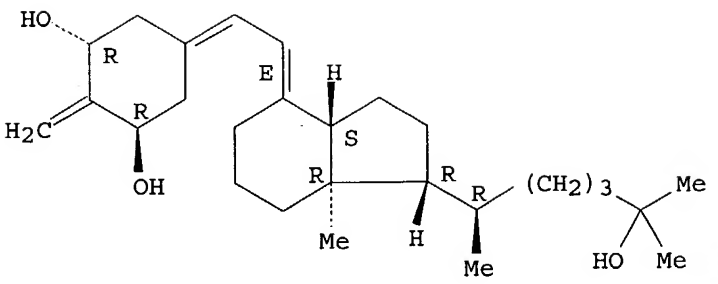
RN 213250-70-5 HCAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 213319-29-0 HCAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Anon	1998			WO 9841501	HCAPLUS
Deluca	1989			US 4800198 A	HCAPLUS
Deluca	1989			US 4851401 A	HCAPLUS
Deluca	1992			US 5089641 A	HCAPLUS
Deluca	1996			US 5587497 A	HCAPLUS
Deluca	1999			US 5945410 A	HCAPLUS
Deluca	1999			US 5981780 A	HCAPLUS
Paaren	1999			US 5936105 A	HCAPLUS
Sicinski	1998		4662	J Med Chem	HCAPLUS
Yang	1999		16838	Journal of Biologica	HCAPLUS

L30 ANSWER 13 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:332679 HCAPLUS
DN 136:335278
TI 1α-Hydroxy-2-methylene-19-nor-homopregnacalciferol and its therapeutic uses
IN **DeLuca, Hector F.**; Sicinski, Rafal R.; Gowlugari, Sumithra; **Plum, Lori A.**; Clagett-Dame, Margaret
PA USA
SO U.S. Pat. Appl. Publ., 14 pp., Cont.-in-part of U. S. Ser. No. 657,828.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

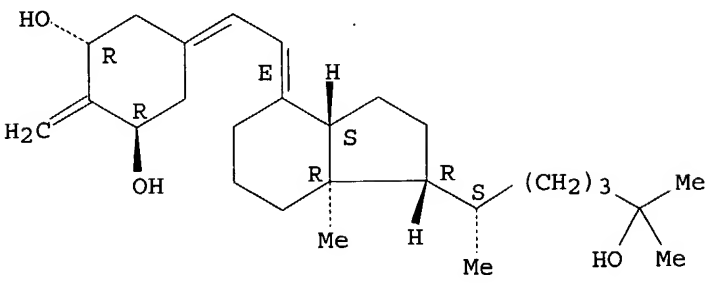
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002052350	A1	20020502	US 2001-878438	20010611
	US 6440953	B2	20020827		
	US 2002183289	A1	20021205	US 2002-165123	20020607
	US 6579861	B2	20030617		
PRAI	US 2000-657828	A2	20000908		
	US 2001-878438	A3	20010611		

AB The invention discloses 1α-hydroxy-2-methylene-19-nor-homopregnacalciferol and its pharmaceutical uses. This compound exhibits pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. This compound also has little, if any, calcemic activity and therefore may be used to treat immune disorders in humans as well as renal osteodystrophy.

IT **213250-70-5**
RL: PAC (Pharmacological activity); BIOL (Biological study)
(hydroxymethylenenorhomopregnacalciferol and therapeutic use)
RN 213250-70-5 HCAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,

(1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L30 ANSWER 14 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:830900 HCAPLUS
DN 135:358086
TI Preparation of 26,27-homologated-20-epi-2-alkyl-19-nor-vitamin D compounds
IN **Deluca, Hector F.**; Sicinski, Rafal R.
PA Wisconsin Alumni Research Foundation, USA
SO U.S., 33 pp., Cont.-in-part of U.S. Ser. No. 454,013.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 6

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6316642	B1	20011113	US 2000-541470	20000331
	US 5945410	A	19990831	US 1997-819694	19970317
	US 6127559	A	20001003	US 1998-135463	19980817
	US 6277837	B1	20010821	US 1999-454013	19991203
	WO 2001074765	A1	20011011	WO 2001-US10094	20010329
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1268415	A1	20030102	EP 2001-920863	20010329
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	JP 2004500414	T2	20040108	JP 2001-572460	20010329
	US 2002123638	A1	20020905	US 2001-999299	20011031
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	US 2003073857	A1	20030417	US 2002-246968	20020919
	US 6667298	B2	20031223		
	US 2004072804	A1	20040415	US 2003-673618	20030929
	US 2004082802	A1	20040429	US 2003-683330	20031010
PRAI	US 1997-819694	A2	19970317		
	US 1998-135463	A3	19980817		
	US 1999-454013	A2	19991203		
	US 2000-541470	A	20000331		
	WO 2001-US10094	W	20010329		
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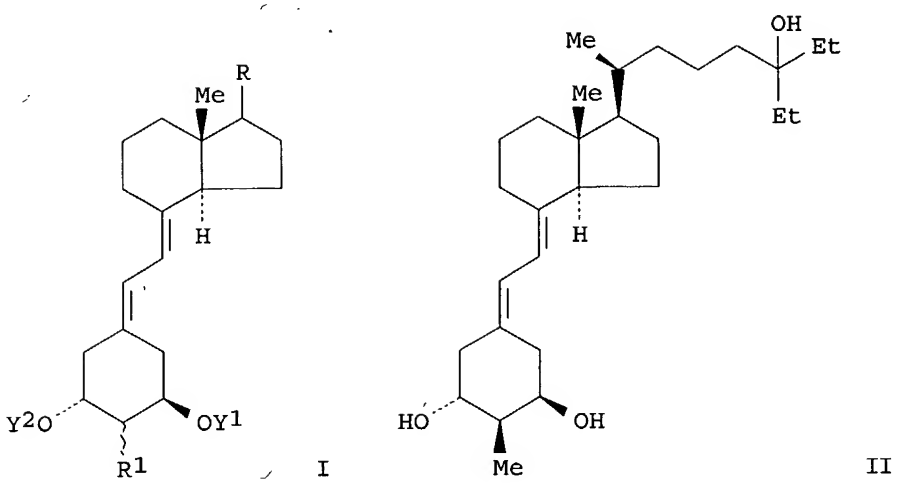
OS MARPAT 135:358086
GI



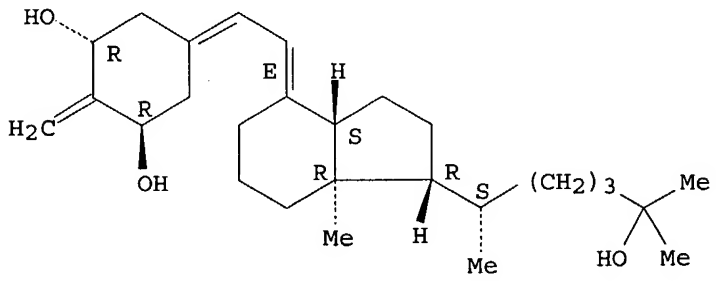
I II

AB 2-Alkyl-19-nor-vitamin D derivs. of formula I [Y1, Y2 = H, protecting group; R = typical side chains known for vitamin D type compds.; R1 = alkyl, hydroxyalkyl, fluoroalkyl] are prepared These 2-substituted compds., especially the 2α-Me and the 2α-methyl-20S derivs., are characterized by relatively high intestinal calcium transport activity and relatively high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. These compds. also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anticancer agents and for the treatment of diseases such as psoriasis. Thus, II was prepared and showed preferential activity on bone in biol. activity tests.

IT **213250-70-5P 213319-29-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 26,27-homologated-20-epi-2-alkyl-19-norvitamin D compds. with high intestinal calcium transport activity)

RN 213250-70-5 HCAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

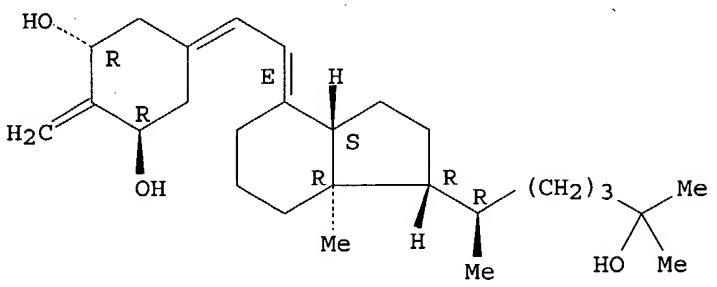
Absolute stereochemistry.
Double bond geometry as shown.



RN 213319-29-0 HCAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,

(1α,3β,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Anon	1985			EP 0184206	HCAPLUS
Anon	1987			EP 0078704	HCAPLUS
Anon	1989				HCAPLUS
Anon	1990			EP 0387077	HCAPLUS
Anon	1990			WO 9009991	HCAPLUS
Anon	1992			EP 0474517	HCAPLUS
Anon	1992			EP 0480572	HCAPLUS
Anon	1992			EP 0516410	HCAPLUS
Anon	1996			WO 9601811	HCAPLUS
Anon	1994	121		Chemical Abstracts	
Baggiolini	1986	51	3098	Journal of Organic C	HCAPLUS
Bouillon	1993	8	1009	Bioactivity of 19-No	HCAPLUS
Brenner	1998			US 5849726	HCAPLUS
Deluca	1992			US 5086191	HCAPLUS
Deluca	1993			US 5237110	HCAPLUS
Deluca	1993			US 5246925	HCAPLUS
Deluca	1996			US 5536713	HCAPLUS
Deluca	1996			US 5587497	HCAPLUS
Deluca	1998			US 5843927	HCAPLUS
Kiegiel	1991	31	6057	Tetrahedron Letters	
Kutner	1998			US 5817648	HCAPLUS
Labrie	1998			US 5846960	HCAPLUS
Miyamoto	1987			US 4666634	HCAPLUS
Miyamoto	1999			US 5877168	HCAPLUS
Okano	1989	163	1444	Biochemical and Biop	HCAPLUS
Perlman	1990	31	1823	Tetrahedron Letters	HCAPLUS
Posner	1995	56	4339	Journal of Organic C	
Posner	1995	60	4617	Journal of Organic C	HCAPLUS
Sarandeses	1992		5445	tetrahedron Letters	HCAPLUS
Sicinski	1998	41	4662	Journal of Medical C	HCAPLUS
Slatopolsky	1995	26	832	American Journal of	

L30 ANSWER 15 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:747743 HCAPLUS
DN 135:288953
TI Preparation of 2-alkylidene-19-nor-vitamin D compounds as antiosteoporotics and antitumor agents
IN **Deluca, Hector F.**; Sicinski, Rafal R.
PA Wisconsin Alumni Research Foundation, USA
SO PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DT Patent

LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001074766	A1	20011011	WO 2001-US10317	20010329
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6392071	B1	20020521	US 2000-540686	20000331
	EP 1268416	A1	20030102	EP 2001-920897	20010329
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2003529581	T2	20031007	JP 2001-572461	20010329
PRAI	US 2000-540686	A	20000331		
	US 1997-819693	A3	19970317		
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	WO 2001-US10317	W	20010329		

OS MARPAT 135:288953
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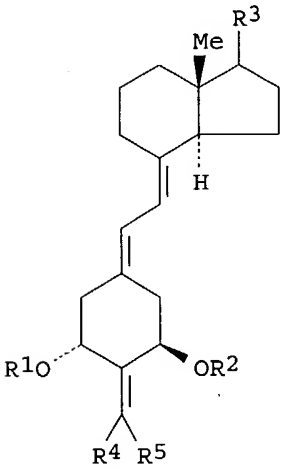

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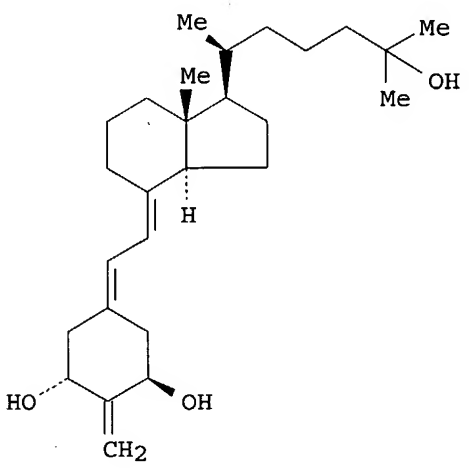


II

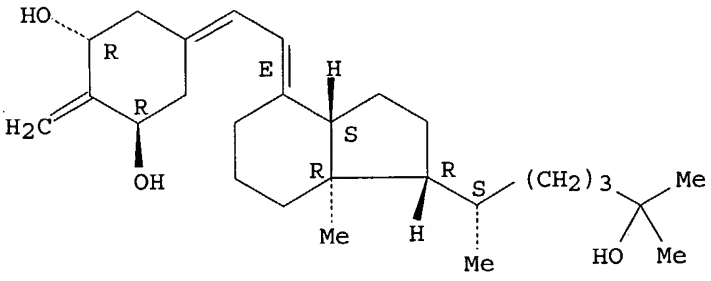
AB Novel vitamin D related compds., namely, 2-alkylidene-19-nor-vitamin D derivs. of formula I [R1, R2 = H, protecting group; R3 = typical side chains known for vitamin D type compds.; R4, R5 = H, alkyl, hydroxyalkyl, fluoroalkyl, etc.; R4R5 = cycloalkylidene] are prepared These 2-substituted compds. are characterized by relatively high intestinal calcium transport activity and relatively high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. These compds. also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anticancer agents and for the treatment of diseases such as psoriasis. Thus, II is prepared and is found to be extremely potent in inducing differentiation of HL-60 cells.

IT **213250-70-5P 213319-29-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-alkylidene-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)

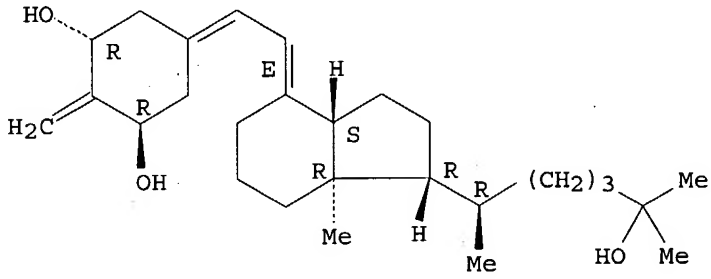
RN 213250-70-5 HCAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 213319-29-0 HCAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Deluca, H	1989			US 4851401 A	HCAPLUS
Deluca, H	1999			US 5981780 A	HCAPLUS
Sicinski	1998	41	4662	JOURNAL OF MEDICINAL	HCAPLUS
Wisconsin Alumni Res Fo	1998			WO 9841501 A	HCAPLUS
Yang	1999	274	16838	J BIOL CHEM	HCAPLUS

L30 ANSWER 16 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:747742 HCAPLUS
DN 135:304063
TI Preparation of 26,27-homologated-20-epi-2-alkyl-19-nor-vitamin D compounds
IN **Deluca, Hector F.**; Sicinski, Rafal R.
PA Wisconsin Alumni Research Foundation, USA
SO PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 6

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001074765	A1	20011011	WO 2001-US10094	20010329
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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	EP 1268415	A1	20030102	EP 2001-920863	20010329
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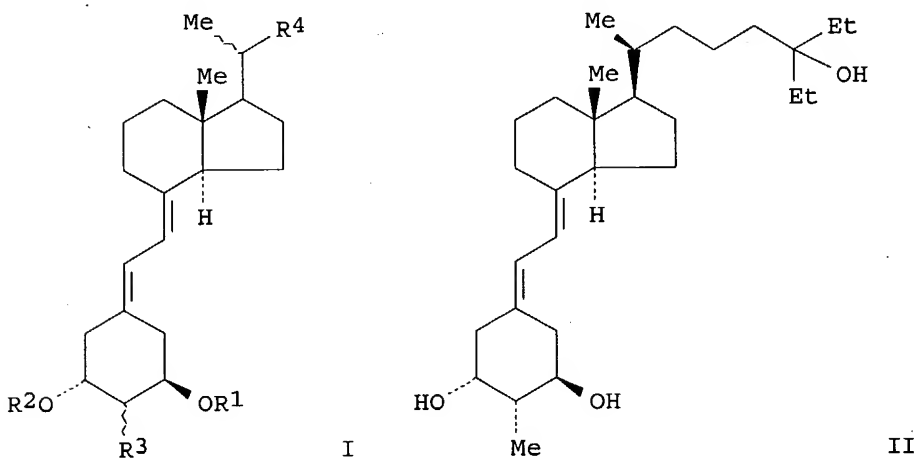
	JP 2004500414	T2	20040108	JP 2001-572460	20010329
	US 2004072804	A1	20040415	US 2003-673618	20030929
PRAI	US 2000-541470	A	20000331		
	US 1997-819694	A2	19970317		
	US 1998-135463	A3	19980817		
	US 1999-454013	A2	19991203		
	WO 2001-US10094	W	20010329		
	US 2001-45941	B3	20011019		
OS	MARPAT 135:304063				
GI					

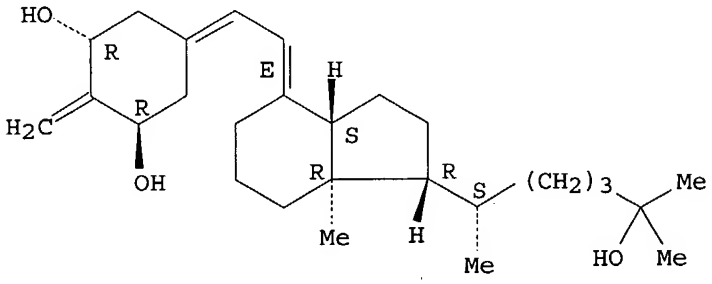


AB 2-Alkyl-19-nor-vitamin D derivs. of formula I [R1, R2 = H, protecting group; R3 = alkyl, hydroxyalkyl, fluoroalkyl; R4 = H, Me, acyl, OH, any of the typical side chains known for vitamin D type compds., etc.] are prepared These compds. are characterized by relatively high intestinal calcium transport activity and relatively high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. These compds. also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis. Thus, II is prepared and had a VDR binding ratio of 5.5, and HL-60 differentiation ED50 of 1.1 x 10-10 M.

IT **213250-70-5P 213319-29-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 26,27-homologated-20-epi-2-alkyl-19-nor-vitamin D compds. as

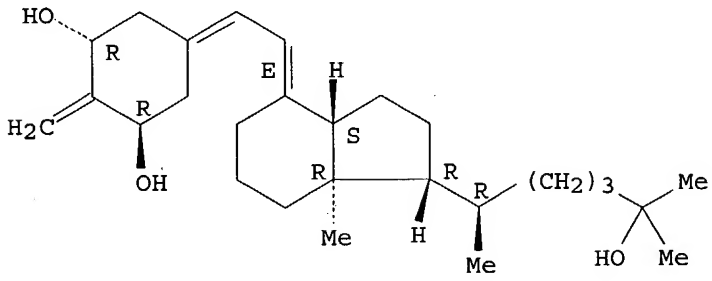
antiosteoporotics and antitumor agents)
RN 213250-70-5 HCAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 213319-29-0 HCAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Mikami, K	1999	12	1899	SYNLETT	
Sicinski, R	1998	41	4662	J MED CHEM	HCAPLUS
Winconsin Alumni Resear	2000			WO 0010548 A	
Wisconsin Alumni Resear	1990			WO 9000541 A	HCAPLUS
Wisconsin Alumni Resear	1998			WO 9841500 A	HCAPLUS

L30 ANSWER 17 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:699222 HCAPLUS
DN 133:267021
TI preparation and therapeutic use of 2-alkyl-19-nor-vitamin D derivatives
IN **Deluca, Hector F.**; Sicinski, Rafal R.
PA Wisconsin Alumni Research Foundation, USA
SO U.S., 27 pp., Cont.-in-part of U.S. 5,945,410.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 6

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 6127559	A	20001003	US 1998-135463	19980817

	US 5945410	A	19990831	US 1997-819694	19970317
	PT 971888	T	20040331	PT 1998-905101	19980211
	ES 2206893	T3	20040516	ES 1998-905101	19980211
	US 6277837	B1	20010821	US 1999-454013	19991203
	US 6316642	B1	20011113	US 2000-541470	20000331
	US 6306844	B1	20011023	US 2000-616778	20000714
	US 2002151528	A1	20021017	US 2001-45941	20011019
	US 2002123638	A1	20020905	US 2001-999299	20011031
	US 6544969	B2	20030408		
	US 2003073857	A1	20030417	US 2002-246968	20020919
	US 6667298	B2	20031223		
	US 2004072804	A1	20040415	US 2003-673618	20030929
	US 2004082802	A1	20040429	US 2003-683330	20031010
PRAI	US 1997-819694	A2	19970317		
	US 1998-135463	A3	19980817		
	US 1999-454013	A2	19991203		
	US 2000-541470	A3	20000331		
	US 2000-616778	A3	20000714		
	JP 2001-83085	A	20010322		
	US 2001-45941	B3	20011019		
	US 2001-999299	A3	20011031		
	US 2002-246968	A3	20020919		

OS MARPAT 133:267021

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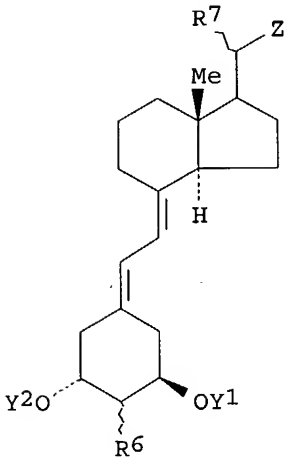

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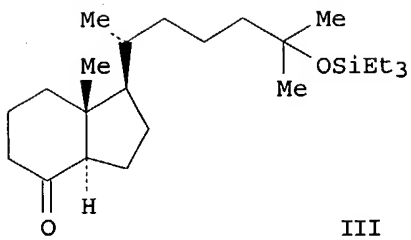


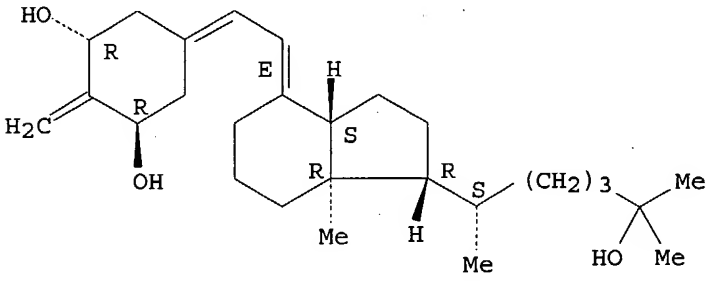
III

AB This invention discloses a novel class of vitamin D related compds., namely, the 2-alkyl-19-nor-vitamin D derivs. (I) (Y1,Y2 = H, hydroxy-protecting group; R6 = alkyl, hydroxyalkyl, fluoroalkyl; R7 = α or β-Me; Z = Y, -OY, -CH2OY, -C.tplbond.CY, -CH=CHY (Y = H, Me, -(CH2)m-C(R1R2)-(CH2)n-C(R3R4R5); where m and n, independently integers from 0-5; R1 = H, OH, protected hydroxy, F, CF3, alkyl etc., R2, R3, R4 = D, deuteroalkyl, H, F, CF3, alkyl etc., R1+R2 = O, =C(R2R3) etc., R5 = H, OH, protected hydroxy, alkyl, and wherein any of the CH-groups at position 20,22, or 23 in the side chain may be replaced by a N atom or where any of the groups -CH(Me)-, -CH(R3)-, or -CH(R2)- at positions 20, 22, and 23, resp., may be replaced by an oxygen or sulfur atom)), were prepared Thus, I (Y1,Y2 = H; R6,R7 = α-Me; Z = (CH2)3C(Me)2OH) (II) was prepared starting from Me quinicate and followed by Wittig-Horner coupling with Grundman's ketone (III). The 2-substituted compds., especially the 2α-Me and the 2α-methyl-20S derivs., are characterized by relatively low intestinal calcium transport activity and high bone calcium mobilization activity resulting in novel therapeutic agents for the

treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. I also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis.

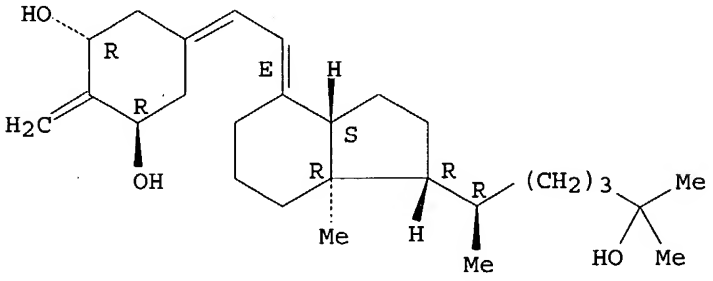
IT **213250-70-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation and therapeutic use of 2-alkyl-19-nor-vitamin D analog)
RN 213250-70-5 HCAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



IT **213319-29-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and therapeutic use of 2-alkyl-19-nor-vitamin D analog)
RN 213319-29-0 HCAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RETABLE

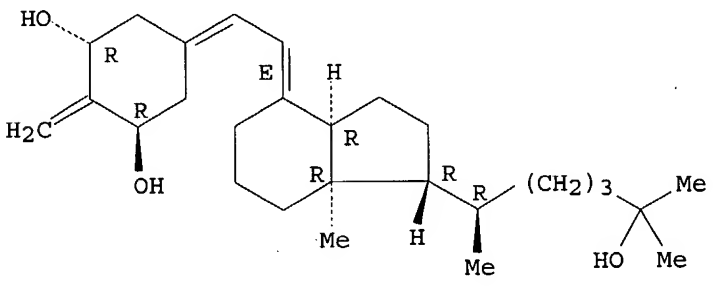
Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Anon	1985			EP 0184206	HCAPLUS
Anon	1990			EP 0387077	HCAPLUS
Anon	1992			EP 0516410	HCAPLUS
Deluca	1992			US 5086191	HCAPLUS
Miyamoto	1987			US 4666634	HCAPLUS
Posner	1991	56	4339	J Org Chem	HCAPLUS

L30 ANSWER 18 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:505692 HCAPLUS
DN 131:144749
TI Preparation of 14-epi-19-nor-vitamin D compounds with cell differentiation activity
IN Paaren, Herbert E.
PA Tetrionics, Inc., USA
SO U.S., 14 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5936105	A	19990810	US 1998-96330	19980611
PRAI US 1997-53088P	P	19970613		

AB 14-Epi-19-nor-vitamin D analog compds. are prepared with high cell differentiation and antiproliferative activity and low calcemic activity. More particularly, examples of such compds. include 14-epi-19-nor-1α,25-dihydroxyvitamin D3, 14-epi-20-epi-19-nor-1α,25-dihydroxyvitamin D3 (I), 14-epi-20-epi-19-nor-1α-hydroxyvitamin D3, 14-epi-19-nor-1α,25-dihydroxyvitamin D2, 14-epi-19-nor-24-homo-1α,25-dihydroxyvitamin D3, 14-epi-19-nor-20(S)-hydroxymethyl-1α-hydroxypregnacalciferol, and 14-epi-19-nor-20(R)-hydroxymethyl-1α-hydroxypregnacalciferol. Thus, I was prepared and showed an EC50 of 0.66 nM to inhibit proliferation of HL-60 cells.
IT **235108-14-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 14-epi-19-nor-vitamin D compds. with cell differentiation activity)
RN 235108-14-2 HCAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,14β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
DeLuca	1995			US 5391755	HCAPLUS
Deluca	1998			US 5843928	HCAPLUS

L30 ANSWER 19 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:672847 HCAPLUS
DN 130:52625
TI New 1α,25-Dihydroxy-19-norvitamin D3 Compounds of High Biological

Activity: Synthesis and Biological Evaluation of 2-Hydroxymethyl, 2-Methyl, and 2-Methylene Analogs

AU Sicinski, Rafal R.; Prahl, Jean M.; Smith, Connie M.; **DeLuca, Hector F.**

CS Department of Biochemistry College of Agricultural and Life Sciences, University of Wisconsin-Madison, Madison, WI, 53706, USA

SO Journal of Medicinal Chemistry (1998), 41(23), 4662-4674
CODEN: JMCMAR; ISSN: 0022-2623

PB American Chemical Society

DT Journal

LA English

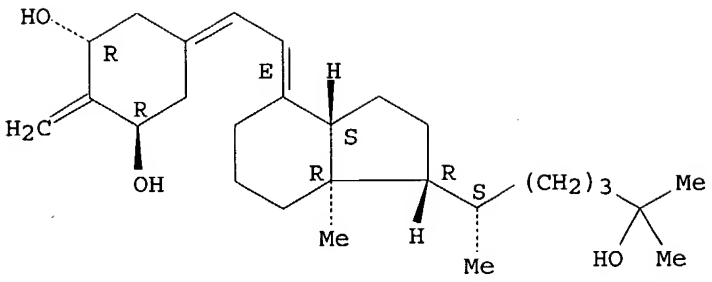
AB New highly active isomers of the natural hormone 1α,25-dihydroxyvitamin D3 possessing an exomethylene group at the 2-position were prepared in a convergent manner, starting with (-)-quinic acid and the corresponding (20R)- and (20S)-25-hydroxy Grundmann ketones. These 2-methylene-19-norvitamins were efficiently converted to the 2-Me and 2-hydroxymethyl derivs., some of which exhibited pronounced in vivo biol. activity. Configurations of the A-ring substituents were determined by 1H NOE difference spectroscopy as well as by spin decoupling expts. It was established that the bulky Me and hydroxymethyl substituents at C-2, due to their large conformational free energies, occupy mainly equatorial positions. Addnl., hydroxylation of the C(10)-C(19) double bond in 1α,25-(OH)2D3 was performed, resulting in 1α,19,25-trihydroxy-10,19-dihydrovitamin D3 derivs. in which the hydroxymethyl substituent at C-10, for steric reasons, is forced to occupy an axial position. In consequence, the vitamin D3 analogs were synthesized in which the 1α-hydroxy group, required for biol. activity, is almost exclusively axially or equatorially oriented because of stabilization of the single A-ring chair conformations. The relative ability of the synthesized analogs to bind the porcine intestinal vitamin D receptor was assessed and compared with that of the natural hormone. It was established that vitamins possessing the axial orientation of the 1α-hydroxy substituent exhibit a significantly increased receptor binding affinity. Compds. with a 2-methylene substituent showed selective calcemic activity profiles, being extremely effective on bone calcium mobilization. 2α-Methyl-substituted vitamins proved to be much more active in vivo than the corresponding epimers with 2β-configuration. All of the 2-substituted vitamins exhibited pronounced HL-60 differentiating activity, those 2α-substituted in the 20S-series being especially potent. The present studies imply that the axial orientation of the 1α-hydroxy group is necessary for biol. activity of vitamin D compds.

IT **213250-70-5P 213319-29-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and biol. evaluation of 2-hydroxymethyl, 2-Me, and 2-methylene 1α,25-dihydroxy-19-norvitamin D3 analogs)

RN 213250-70-5 HCAPLUS

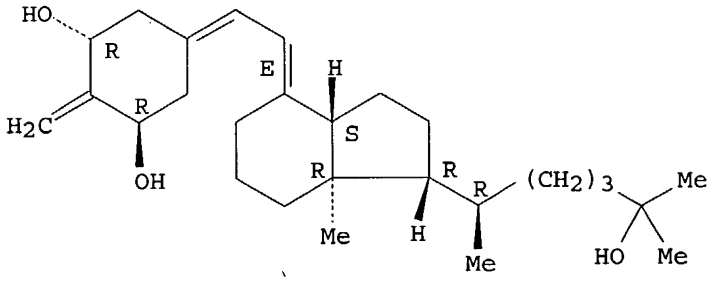
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 213319-29-0 HCAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Anet, F	1962	84	1053	J Am Chem Soc	HCAPLUS
Berman, E	1978	100	5626	J Am Chem Soc	HCAPLUS
Berman, E	1977	42	3325	J Org Chem	MEDLINE
Binderup, L	1991	42	1569	Biochem Pharmacol	HCAPLUS
Bouillon, R	1995	16	200	Endocr Rev	HCAPLUS
Dame, M	1986	25	4523	Biochemistry	HCAPLUS
Deluca, H				EP 387077	HCAPLUS
Deluca, H	1984	19	179	Annu Rep Med Chem	HCAPLUS
Deluca, H	1991	3	1129	Comprehensive Medici	
Deluca, H	1988	2	224	FASEB J	HCAPLUS
Deluca, H	1974	33	2211	Fed Proc	HCAPLUS
Deluca, H	1979	83	1	Top Curr Chem	HCAPLUS
Eguchi, T	1990	18	19	Bioorg Chem	HCAPLUS
Eguchi, T	1991	19	327	Bioorg Chem	HCAPLUS
Eliel, E	1965		355	Conformational Analy	
Havinga, E	1973	29	1181	Experientia	HCAPLUS
Helmer, B	1985	241	608	Arch Biochem Biophys	HCAPLUS
Hirsch, J	1967	1	199	Top Stereochem	HCAPLUS
Ikekawa, N	1987	7	333	Med Res Rev	HCAPLUS
Ikekawa, N	1987	7	333	Med Res Rev	HCAPLUS
Ishida, H	1995	60	1828	J Org Chem	HCAPLUS
Johnson, F	1968	68	375	Chem Rev	HCAPLUS
Johnson, F	1965	87	5492	J Am Chem Soc	HCAPLUS
Jones, G	1987	49	29	Steroids	HCAPLUS
Konno, K	1998	8	151	Bioorg Med Chem Lett	HCAPLUS
Kragballe, K	1992	49	46	J Cell Biochem	HCAPLUS
Lythgoe, B	1981		449	Chem Soc Rev	

Lythgoe, B	1976		2386	J Chem Soc Perkin Tr	HCAPLUS
Lythgoe, B	1978		590	J Chem Soc Perkin Tr	HCAPLUS
Maclaughlin, J	1985	82	5409	Proc Natl Acad Sci U	HCAPLUS
Miyamoto, K				EP 184206	HCAPLUS
Miyamoto, K	1993	41	1111	Chem Pharm Bull	HCAPLUS
Miyaura, C	1981	102	937	Biochem Biophys Res	HCAPLUS
Morimoto, S	1986	38	119	Calcif Tissue Int	MEDLINE
Mourino, A	1978	43	1653	J Org Chem	HCAPLUS
Narwid, T	1974	57	771	Helv Chim Acta	HCAPLUS
Nasipuri, D	1991		270	Stereochemistry of o	
Nordin, B	1992	49	19	J Cell Biochem	HCAPLUS
Norman, A	1994			Vitamin D, a pluripo	
Norman, A	1979			Vitamin D the calciu	
Okamura, W	1977	42	2284	J Org Chem	HCAPLUS
Okamura, W	1978	43	574	J Org Chem	HCAPLUS
Okamura, W	1995	53	603	J Steroid Biochem Mo	HCAPLUS
Okamura, W	1974	71	4194	Proc Natl Acad Sci U	HCAPLUS
Okamura, W	1975		4317	Tetrahedron Lett	HCAPLUS
Okano, T	1989	163	1444	Biochem Biophys Res	HCAPLUS
Ostrem, V	1987	262	14164	J Biol Chem	HCAPLUS
Ostrem, V	1987	49	73	Steroids	HCAPLUS
Paaren, H	1985	13	62	Bioorg Chem	HCAPLUS
Perlman, K	1990	31	1823	Tetrahedron Lett	HCAPLUS
Perlman, K	1991	32	7663	Tetrahedron Lett	HCAPLUS
Posner, G	1994	59	7855	J Org Chem	HCAPLUS
Posner, G	1995	60	4617	J Org Chem	HCAPLUS
Reichel, H	1989	320	980	N Engl J Med	HCAPLUS
Schlosser, M	1976	30	197	Chimia	HCAPLUS
Sheves, M	1975		643	J Chem Soc Chem Comm	HCAPLUS
Sheves, M	1977	42	3597	J Org Chem	HCAPLUS
Sicinski, R	1994	22	150	Bioorg Chem	HCAPLUS
Sicinski, R	1994	37	3730	J Med Chem	HCAPLUS
Snedecor, G	1967			Statistical Methods	
Stoddart, J	1971		64	Stereochemistry of c	
Suda, T	1990	10	195	Annu Rev Nutr	HCAPLUS
Suda, T	1970	100	1049	J Nutr	HCAPLUS
Suda, T	1989	191	214	Proc Soc Exp Biol Me	HCAPLUS
Tsoukas, C	1984	224	1438	Science (Washington,	HCAPLUS
Uhland-Smith, A	1993	123	1777	J Nutr	HCAPLUS
van der Kerkhof, P	1995	132	675	Br J Dermatol	
Wecksler, W	1980	35	419	Steroids	HCAPLUS
Wing, R	1975	97	4980	J Am Chem Soc	HCAPLUS
Winstein, S	1955	77	5562	J Am Chem Soc	HCAPLUS

L30 ANSWER 20 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:635741 HCAPLUS
DN 129:245333
TI Preparation of 2-alkylidene-19-nor-vitamin D compounds
IN **Deluca, Hector F.**; Sicinski, Rafal R.
PA Wisconsin Alumni Research Foundation, USA
SO PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9841501	A1	19980924	WO 1998-US2976	19980211

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GW, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

	US 5843928	A	19981201	US 1997-819693	19970317
	AU 9862801	A1	19981012	AU 1998-62801	19980211
	AU 714253	B2	19991223		
	EP 970047	A1	20000112	EP 1998-905102	19980211
	EP 970047	B1	20020911		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	NZ 337503	A	20000929	NZ 1998-337503	19980211
	JP 2001504135	T2	20010327	JP 1998-540501	19980211
	AT 223890	E	20020915	AT 1998-905102	19980211
	ES 2179451	T3	20030116	ES 1998-905102	19980211
	PT 970047	T	20030131	PT 1998-905102	19980211
	NO 9904398	A	19990910	NO 1999-4398	19990910
PRAI	US 1997-819693	A	19970317		
	WO 1998-US2976	W	19980211		

OS MARPAT 129:245333
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

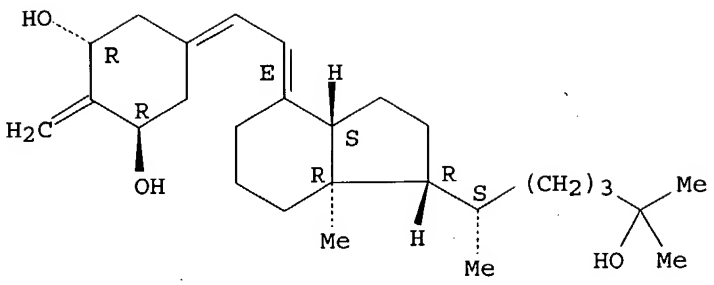
AB The title compds. [I; Y1, Y2 = H, protecting group; R6, R8 = H, alkyl, hydroxyalkyl, fluoroalkyl, or R6R8 = (CH2)x; x = 2-5 integer; R = any of the typical side chains known for vitamin D type compds., e.g. Q] are prepared Thus, 1α,25-dihydroxy-2-methylene-19-norvitamin D3 (II) was prepared in 11 steps from (-)-quinic acid via tert-butyldimethylsilyl protection of the OH groups at the 3 and 5 positions, converting to protected quinic acid Me ester, oxidation of the 4-OH, methylenation using methyltriphenylphosphonium bromide, hydride reduction, NaIO4 oxidation, condensation of 3,5-bis(tert-butyldimethylsilyloxy)-4-methylenecyclohexanone with Me3SiCH2-COOMe, DIBAL reduction, reaction with Ph2PH, H2O2 oxidation, condensation with perhydroindanone III in the presence of BuLi, and deprotection. These 2-substituted compds. are characterized by low intestinal calcium transport activity and high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. The intestinal calcium transport and serum calcium (bone calcium mobilization) activities in rats responding to chronic doses of II at 130 pmol/day/7 days were 5.3±0.4 S/M and 9.9±0.2 mg/100 Ml, resp., vs. 6.2±0.4 S/M and 7.2±0.5 mg/100 mL, resp., for 1,25-(OH)2D3. These compds. also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis.

IT **213250-70-5P**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-alkylidenenor-vitamin D compds.)

RN 213250-70-5 HCAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Chugai Pharmaceutical C	1994			JP 06041059 A	HCAPLUS
Deluca, H	1996			US 5536713 A	HCAPLUS
Miyamoto, K	1987			US 4666634 A	HCAPLUS
The John-Hopkins Univer	1996			WO 9601811 A	HCAPLUS

L30 ANSWER 21 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:635740 HCAPLUS
DN 129:245332
TI Preparation of 2-alkyl-19-nor-vitamin D compounds and their biological activities
IN **Deluca, Hector F.**; Sicinski, Rafal R.
PA Wisconsin Alumni Research Foundation, USA
SO PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 6

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9841500	A1	19980924	WO 1998-US2975	19980211
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	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 5945410	A	19990831	US 1997-819694	19970317
	AU 9862800	A1	19981012	AU 1998-62800	19980211
	AU 714390	B2	19991223		
	EP 971888	A1	20000119	EP 1998-905101	19980211
	EP 971888	B1	20031029		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	BR 9808010	A	20000308	BR 1998-8010	19980211
	NZ 337262	A	20000929	NZ 1998-337262	19980211
	JP 2000513010	T2	20001003	JP 1998-540500	19980211
	AT 253046	E	20031115	AT 1998-905101	19980211
	PT 971888	T	20040331	PT 1998-905101	19980211
	ES 2206893	T3	20040516	ES 1998-905101	19980211
	NO 9904489	A	19990916	NO 1999-4489	19990916
	US 2004072804	A1	20040415	US 2003-673618	20030929
PRAI	US 1997-819694	A	19970317		
	WO 1998-US2975	W	19980211		
	US 2001-45941	B3	20011019		

OS MARPAT 129:245332
GI

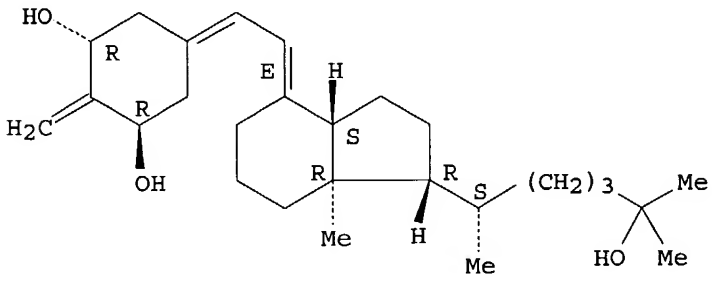
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; Y1, Y2 = H, protecting group; R6 = alkyl, hydroxyalkyl, fluoroalkyl, etc.; R = any of the typical side chains known for vitamin D type compds., e.g. Q] are prepared Thus, 1α,25-dihydroxy-2α- and 1α,25-dihydroxy-2β-methyl-19-norvitamin D3 (II) were prepared in 11 steps from (-)-quinic acid via tert-butyldimethylsilyl protection of the OH groups at positions 3 and 5, converting to protected quinic acid Me ester, oxidation of the 4-OH, methylenation using methyltriphenylphosphonium bromide, hydride reduction, NaIO4 oxidation, condensation of the resulting 3,5-bis(tert-butyldimethylsilyloxy)-4-methylcyclohexanone with Me3SiCH2COOMe, DIBAL reduction, reaction with Ph2PH, oxidation, condensation with perhydroindanone III in the presence of BuLi, and deprotection. These 2-substituted compds. are characterized by low intestinal calcium transport activity and high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. The intestinal calcium transport and serum calcium (bone calcium mobilization) activities in rats responding to chronic doses of II (both epimers) at 130 pmol/day/7 days were 5.0±0.3 S/M and 6.1±0.1 mg/100 mL, resp., vs. 6.2±0.4 S/M and 7.2±0.5 mg/100 mL, resp., for 1,25-(OH)2D3. These compds. also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis.

IT **213250-70-5P 213319-29-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 2-alkylnor-vitamin D compds. and their biol. activities)

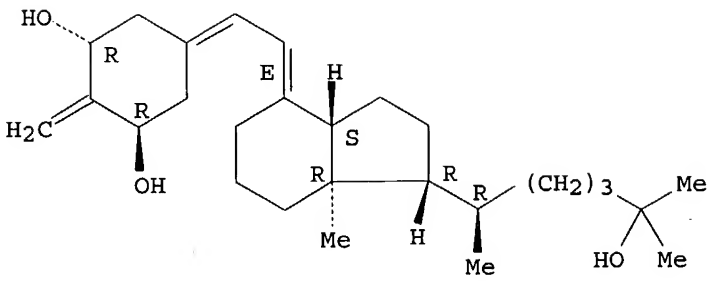
RN 213250-70-5 HCAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 213319-29-0 HCAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Chugai Pharmaceutical C	1994			JP 06041059 A	HCAPLUS
Deluca, H	1996			US 5536713 A	HCAPLUS
Miyamoto, K	1987			US 4666634 A	HCAPLUS
The John-Hopkins Univer	1996			WO 9601811 A	HCAPLUS

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CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPAT2' ENTERED AT 13:51:17 ON 05 SEP 2004
CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

=> => d his l31-

(FILE 'USPATFULL, USPAT2' ENTERED AT 13:51:17 ON 05 SEP 2004)
L31 0 S L29 AND LIFE(L)EXPECT?
L32 2 S L29 AND (AGING? OR AGEING? OR LONGEV?)/CT,BI
L33 22 S L29 NOT L32

=> d l32 bib abs kwic hitstr tot

L32 ANSWER 1 OF 2 USPATFULL on STN
AN 2004:89152 USPATFULL
TI Use of 2-methylene-19-nor-20(S)-1alpha,25-dihydroxyvitamin D3 to increase bone strength
IN DeLuca, Hector F., Deerfield, WI, UNITED STATES
Smith, Connie M., Blue Mounds, WI, UNITED STATES
PI US 2004068129 A1 20040408
AI US 2003-673629 A1 20030929 (10)
RLI Division of Ser. No. US 2000-616164, filed on 14 Jul 2000, PENDING
DT Utility
FS APPLICATION
LREP ANDRUS, SCEALES, STARKE & SAWALL, LLP, 100 EAST WISCONSIN AVENUE, SUITE 1100, MILWAUKEE, WI, 53202
CLMN Number of Claims: 29
ECL Exemplary Claim: 1
DRWN 7 Drawing Page(s)
LN.CNT 529
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides pharmaceutical uses for 2-methylene-19-nor-20(S)-1α,25-dihydroxyvitamin D.sub.3. This compound is characterized by high bone calcium mobilization activity demonstrating preferential activity on bone. This results in a novel therapeutic agent for the treatment of diseases where bone formation is desired, particularly osteoporosis. This compound also exhibits pronounced activity in arresting the proliferation of undifferentiated cells and inducing their

differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis. This compound also increases both breaking strength and crushing strength of bones evidencing use in conjunction with bone replacement surgery such as hip and knee replacements.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT **Aging, animal**
(senile osteoporosis; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)

IT 32222-06-3, 1α,25-Dihydroxyvitamin D3 **213319-29-0**
(methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)

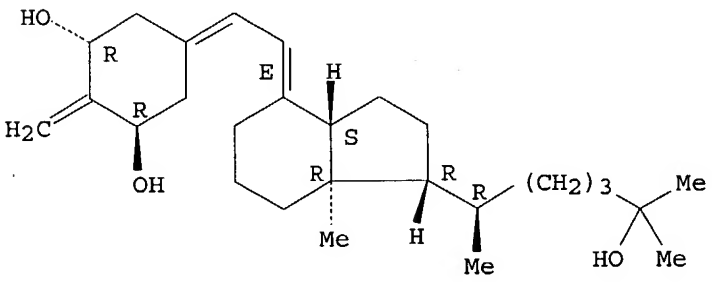
IT **213250-70-5**
(methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)

IT **213319-29-0**
(methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)

RN 213319-29-0 USPATFULL

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

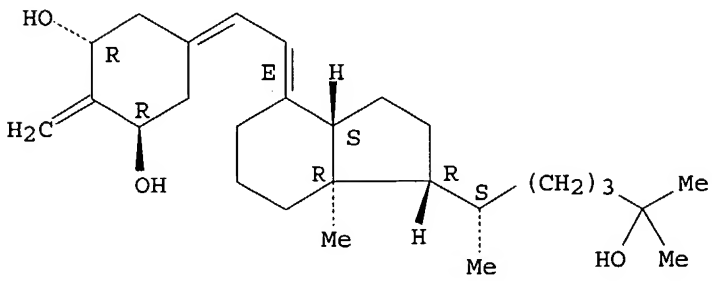


IT **213250-70-5**
(methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)

RN 213250-70-5 USPATFULL

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



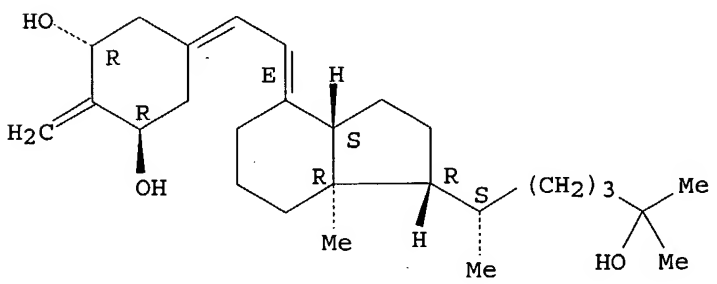
L32 ANSWER 2 OF 2 USPATFULL on STN

AN 2003:277148 USPATFULL

TI Use of carbon-2-modified-vitamin D analogs to induce the formation of new bone
IN DeLuca, Hector F., Deerfield, WI, UNITED STATES
Pike, J. Wesley, Madison, WI, UNITED STATES
Shevde, Nirupama K., Madison, WI, UNITED STATES
PI US 2003195175 A1 20031016
AI US 2002-105826 A1 20020325 (10)
DT Utility
FS APPLICATION
LREP ANDRUS, SCEALES, STARKE & SAWALL, LLP, 100 EAST WISCONSIN AVENUE, SUITE 1100, MILWAUKEE, WI, 53202
CLMN Number of Claims: 28
ECL Exemplary Claim: 1
DRWN 2 Drawing Page(s)
LN.CNT 1018
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB It has been discovered that the 2-carbon-modified derivatives of 1α,25-dihydroxyvitamin D.sub.3 specifically stimulate osteoblasts to form new bone. The ability of the 2-carbon-modified vitamin D analogs to stimulate new bone formation suggest that these compounds can be used where synthesis of new bone is required. Thus, these compounds can be used either systemically or locally to stimulate the growth of bone transplants, to increase the rate of fracture healing and thereby reduce the time required for the healing of fractures, the stimulation of bone growth when required for replacement surgery, and also for the growth of bone to implants or other devices required to maintain the skeleton or teeth in the proper positions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . process that is homeostatic in nature and necessary for renewal of defective bone that occurs as a result of normal **aging** or trauma. This process is essential to the maintenance of adult skeletal integrity and is carried out through the activity. . .
IT 32222-06-3, 1α,25-Dihydroxyvitamin D3 **213250-70-5**
606973-78-8 606973-79-9 606973-80-2 606973-81-3
(use of carbon-2-modified-vitamin D analogs to induce the formation of new bone)
IT **213250-70-5**
(use of carbon-2-modified-vitamin D analogs to induce the formation of new bone)
RN 213250-70-5 USPATFULL
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



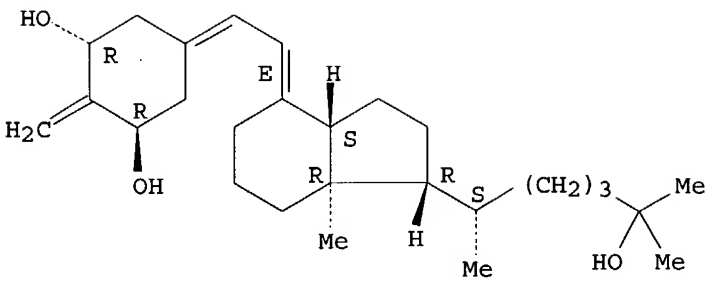
=> d 133 bib abs hitstr tot

L33 ANSWER 1 OF 22 USPATFULL on STN
AN 2004:108400 USPATFULL
TI 26,27-Homologated-20-EPI-2-alkyl-19-nor-vitamin D compounds
IN DeLuca, Hector F., Deerfield, WI, UNITED STATES
Sicinski, Rafal R., Warsaw, POLAND
PA Wisconsin Alumni Research Foundation, Madison, WI (U.S. corporation)
PI US 2004082802 A1 20040429
AI US 2003-683330 A1 20031010 (10)
RLI Division of Ser. No. US 2002-246968, filed on 19 Sep 2002, GRANTED, Pat. No. US 6667298 Division of Ser. No. US 2001-999299, filed on 31 Oct 2001, GRANTED, Pat. No. US 6544969 Division of Ser. No. US 2000-541470, filed on 31 Mar 2000, GRANTED, Pat. No. US 6316642 Continuation-in-part of Ser. No. US 1999-454013, filed on 3 Dec 1999, GRANTED, Pat. No. US 6277837 Division of Ser. No. US 1998-135463, filed on 17 Aug 1998, GRANTED, Pat. No. US 6127559 Continuation-in-part of Ser. No. US 1997-819694, filed on 17 Mar 1997, GRANTED, Pat. No. US 5945410
DT Utility
FS APPLICATION
LREP ANDRUS, SCEALES, STARKE & SAWALL, LLP, 100 EAST WISCONSIN AVENUE, SUITE 1100, MILWAUKEE, WI, 53202
CLMN Number of Claims: 46
ECL Exemplary Claim: 1
DRWN 6 Drawing Page(s)
LN.CNT 2099
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides a novel class of vitamin D related compounds, namely, the 2-alkyl-19-nor-vitamin D derivatives, as well as a general method for their chemical synthesis. The compounds have the formula: ##STR1##

where Y.sub.1 and Y.sub.2, which may be the same or different, are each selected from the group consisting of hydrogen and a hydroxy-protecting group, R.sub.6 is selected from the group consisting of alkyl, hydroxyalkyl and fluoroalkyl, and where the group R represents any of the typical side chains known for vitamin D type compounds. These 2-substituted compounds, especially the 2α-methyl and the 2α-methyl-20S derivatives, are characterized by relatively high intestinal calcium transport activity and relatively high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. These compounds also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis.

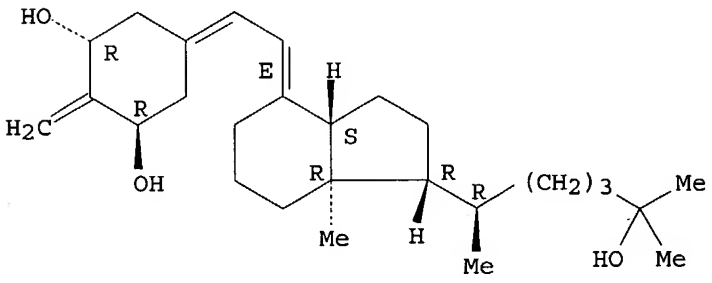
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **213250-70-5P 213319-29-0P**
(preparation of 2-alkylnor-vitamin D compds. and their biol. activities)
RN 213250-70-5 USPATFULL
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 213319-29-0 USPATFULL
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

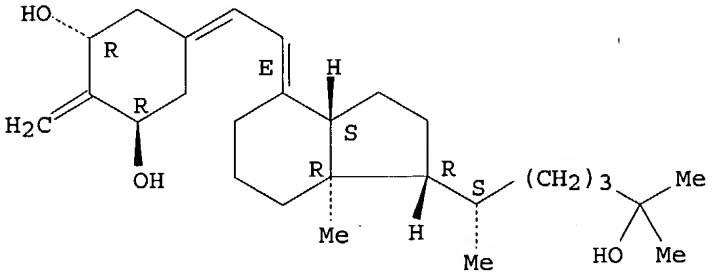


L33 ANSWER 2 OF 22 USPATFULL on STN
AN 2004:95349 USPATFULL
TI Use of 2alpha-methly-19-nor-20(S)-1alpha,25-dihydroxyvitamin D3 to increase bone strength
IN DeLuca, Hector F., Deerfield, WI, UNITED STATES
Smith, Connie M., Blue Mounds, WI, UNITED STATES
PA Wisconsin Alumni Research Foundation (U.S. corporation)
PI US 2004072804 A1 20040415
AI US 2003-673618 A1 20030929 (10)
RLI Division of Ser. No. US 2001-45941, filed on 19 Oct 2001, ABANDONED
DT Utility
FS APPLICATION
LREP ANDRUS, SCEALES, STARKE & SAWALL, LLP, 100 EAST WISCONSIN AVENUE, SUITE 1100, MILWAUKEE, WI, 53202
CLMN Number of Claims: 29
ECL Exemplary Claim: 1
DRWN 3 Drawing Page(s)
LN.CNT 534
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides pharmaceutical uses for 2α-methyl-19-nor-20(S)-1α,25-dihydroxyvitamin D.sub.3. This compound is characterized by high bone calcium mobilization activity demonstrating preferential activity on bone. This results in a novel therapeutic agent for the treatment of diseases where bone formation is desired, particularly osteoporosis. This compound also exhibits pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis. This compound also increases both breaking strength and crushing strength of bones evidencing use in conjunction with bone

replacement surgery such as hip and knee replacements.

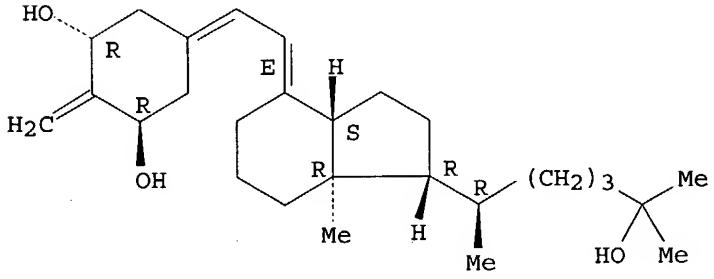
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **213250-70-5P 213319-29-0P**
(preparation of 2-alkylnor-vitamin D compds. and their biol. activities)
RN 213250-70-5 USPATFULL
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 213319-29-0 USPATFULL
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

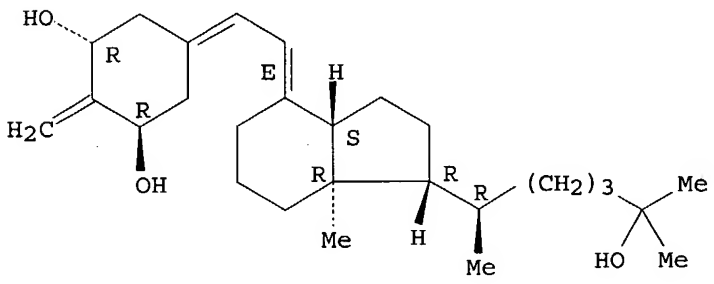


L33 ANSWER 3 OF 22 USPATFULL on STN
AN 2004:70585 USPATFULL
TI Method of extending the dose range of vitamin D compounds
IN DeLuca, Hector F., Deerfield, WI, UNITED STATES
Pike, John W., Madison, WI, UNITED STATES
Shevde, Nirupama, Madison, WI, UNITED STATES
Plum, Lori A., Madison, WI, UNITED STATES
Clagett-Dame, Margaret, Deerfield, WI, UNITED STATES
PI US 2004053813 A1 20040318
AI US 2002-235244 A1 20020905 (10)
DT Utility
FS APPLICATION
LREP ANDRUS, SCEALES, STARKE & SAWALL, LLP, 100 EAST WISCONSIN AVENUE, SUITE 1100, MILWAUKEE, WI, 53202
CLMN Number of Claims: 68
ECL Exemplary Claim: 1
DRWN 2 Drawing Page(s)
LN.CNT 1122
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Inhibitors of bone calcium resorption are administered to allow high doses of vitamin D compounds or mimetics to be given with the intent of treating non-calcium related diseases such as cancer, psoriasis, and autoimmune disease without the dangers of calcification of kidney, heart, and aorta. Inhibitors of bone calcium resorption include the bis-phosphonates, OPG or the soluble RANKL receptor known as sRANK, and function to block the availability of calcium from bone thereby preventing hypercalcemia and the resulting calcification of soft tissues. Thus, high doses of 1α,25-dihydroxyvitamin D.sub.3 (1,25-(OH).sub.2D.sub.3), its analogs, prodrugs, or mimetics can be utilized with minimal risk to a patient. Specifically, alendronate is shown to block the bone calcium mobilization activity of both 1,25-(OH).sub.2D.sub.3 and its very potent analog, 2-methylene-19-nor-(20S)-1α,25-dihydroxyvitamin D.sub.3.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **213319-29-0**
(method of extending dose range of vitamin D compds.)
RN 213319-29-0 USPATFULL
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L33 ANSWER 4 OF 22 USPATFULL on STN
AN 2003:258374 USPATFULL
TI 26,27-homologated-20-EPI-2-alkylidene-19-nor-vitamin D compounds
IN DeLuca, Hector F., Deerfield, WI, UNITED STATES
Sicinski, Rafal R., Warsaw, POLAND
PA Wisconsin Alumni Research Foundation, Madison, WI, UNITED STATES (U.S. corporation)
PI US 2003181427 A1 20030925
US 6696431 B2 20040224
AI US 2003-352745 A1 20030128 (10)
RLI Division of Ser. No. US 2001-1711, filed on 31 Oct 2001, GRANTED, Pat. No. US 6537981 Division of Ser. No. US 2000-540686, filed on 31 Mar 2000, GRANTED, Pat. No. US 6392071 Continuation of Ser. No. US 1999-370966, filed on 10 Aug 1999, ABANDONED Continuation of Ser. No. US 1998-151113, filed on 10 Sep 1998, GRANTED, Pat. No. US 5936133 Division of Ser. No. US 1997-819693, filed on 17 Mar 1997, GRANTED, Pat. No. US 5843928
DT Utility
FS APPLICATION
LREP ANDRUS, SCEALES, STARKE & SAWALL, LLP, 100 EAST WISCONSIN AVENUE, SUITE 1100, MILWAUKEE, WI, 53202
CLMN Number of Claims: 48
ECL Exemplary Claim: 1
DRWN 2 Drawing Page(s)
LN.CNT 1598

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention provides a novel class of vitamin D related compounds, namely, the 2-alkylidene-19-nor-vitamin D derivatives, as well as a general method for their chemical synthesis. The compounds have the formula: ##STR1##

where Y.sub.1 and Y.sub.2, which may be the same or different, are each selected from the group consisting of hydrogen and a hydroxy-protecting group, R.sub.6 and R.sub.8, which may be the same or different, are each selected from hydrogen, alkyl, hydroxyalkyl and fluoroalkyl, or when taken together represent the group --(CH.sub.2).sub.x-- where x is an integer from 2 to 5, and where the group R represents any of the typical side chains known for vitamin D type compounds. These 2-substituted compounds are characterized by relatively high intestinal calcium transport activity and relatively high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. These compounds also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis.

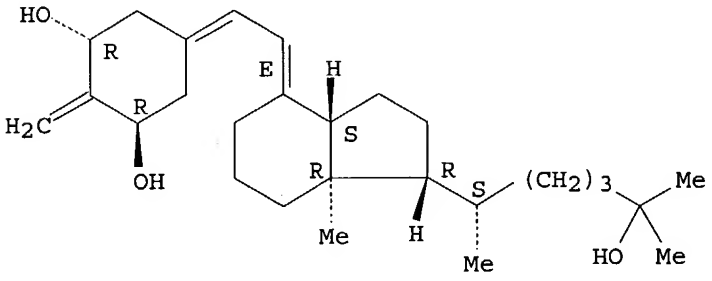
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT **213250-70-5P**
(preparation of 2-alkylidenenor-vitamin D compds.)

RN 213250-70-5 USPATFULL

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L33 ANSWER 5 OF 22 USPATFULL on STN

AN 2003:106944 USPATFULL

TI 26,27-Homologated-20-epi-2-alkyl-19-nor-vitamin D compounds

IN DeLuca, Hector F., Deerfield, WI, UNITED STATES
Sicinski, Rafal R., Warsaw, POLAND

PI US 2003073857 A1 20030417
US 6667298 B2 20031223

AI US 2002-246968 A1 20020919 (10)

RLI Division of Ser. No. US 2001-999299, filed on 31 Oct 2001, PENDING Division of Ser. No. US 2000-541470, filed on 31 Mar 2000, GRANTED, Pat. No. US 6316642 Continuation-in-part of Ser. No. US 1999-454013, filed on 3 Dec 1999, GRANTED, Pat. No. US 6277837 Division of Ser. No. US 1998-135463, filed on 17 Aug 1998, GRANTED, Pat. No. US 6127559 Continuation-in-part of Ser. No. US 1997-819694, filed on 17 Mar 1997, GRANTED, Pat. No. US 5945410

DT Utility

FS APPLICATION

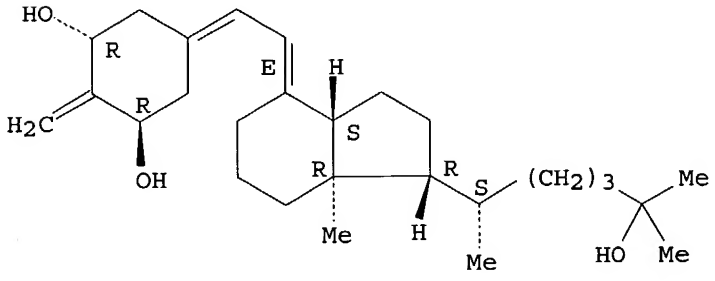
LREP ANDRUS, SCEALES, STARKE & SAWALL, LLP, 100 EAST WISCONSIN AVENUE, SUITE

1100, MILWAUKEE, WI, 53202
CLMN Number of Claims: 46
ECL Exemplary Claim: 1
DRWN 6 Drawing Page(s)
LN.CNT 2101
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides a novel class of vitamin D related compounds, namely, the 2-alkyl-19-nor-vitamin D derivatives, as well as a general method for their chemical synthesis. The compounds have the formula: ##STR1##

where Y.sub.1 and Y.sub.2, which may be the same or different, are each selected from the group consisting of hydrogen and a hydroxy-protecting group, R.sub.6 is selected from the group consisting of alkyl, hydroxyalkyl and fluoroalkyl, and where the group R represents any of the typical side chains known for vitamin D type compounds. These 2-substituted compounds, especially the 2α-methyl and the 2α-methyl-20S derivatives, are characterized by relatively high intestinal calcium transport activity and relatively high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. These compounds also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis.

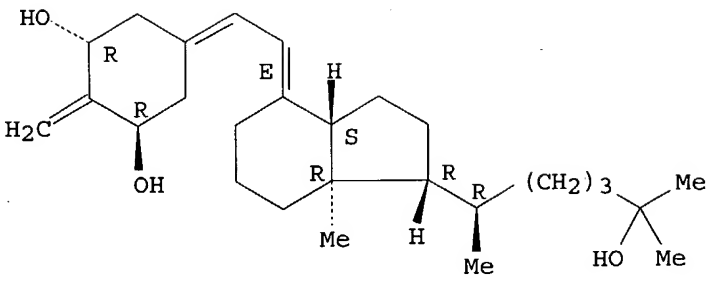
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **213250-70-5P 213319-29-0P**
(preparation of 2-alkylnor-vitamin D compds. and their biol. activities)
RN 213250-70-5 USPATFULL
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 213319-29-0 USPATFULL
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

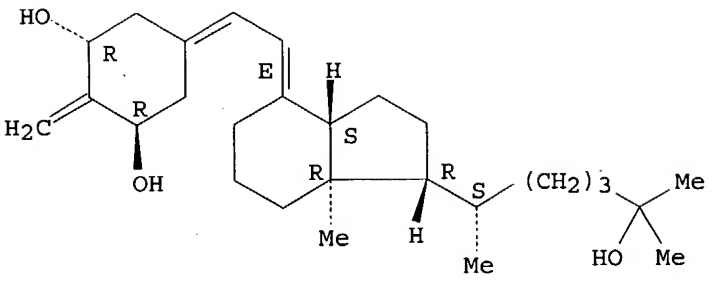
Absolute stereochemistry.
Double bond geometry as shown.



L33 ANSWER 6 OF 22 USPATFULL on STN
AN 2002:273400 USPATFULL
TI Use of 2alpha-methyl-19-nor-20(S)-1alpha,25-dihydroxyvitamin D3 to increase bone strength
IN DeLuca, Hector F., Deerfield, WI, UNITED STATES
Smith, Connie M., Blue Mounds, WI, UNITED STATES
PI US 2002151528 A1 20021017
AI US 2001-45941 A1 20011019 (10)
RLI Division of Ser. No. US 2000-616778, filed on 14 Jul 2000, GRANTED, Pat. No. US 6306844 Continuation-in-part of Ser. No. US 1998-135463, filed on 17 Aug 1998, GRANTED, Pat. No. US 6127559 Continuation-in-part of Ser. No. US 1997-819694, filed on 17 Mar 1997, GRANTED, Pat. No. US 5945410
PRAI JP 2001-83085 20010322
DT Utility
FS APPLICATION
LREP Thomas M. Wozny, ANDRUS, SCEALES, STARKE & SAWALL, LLP, Suite 1100, 100 East Wisconsin Avenue, Milwaukee, WI, 53202-4178
CLMN Number of Claims: 29
ECL Exemplary Claim: 1
DRWN 3 Drawing Page(s)
LN.CNT 532
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides pharmaceutical uses for 2α-methyl-19-nor-20(S)-1α,25-dihydroxyvitamin D.sub.3. This compound is characterized by high bone calcium mobilization activity demonstrating preferential activity on bone. This results in a novel therapeutic agent for the treatment of diseases where bone formation is desired, particularly osteoporosis. This compound also exhibits pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocle thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis. This compound also increases both breaking strength and crushing strength of bones evidencing use in conjunction with bone replacement surgery such as hip and knee replacements.

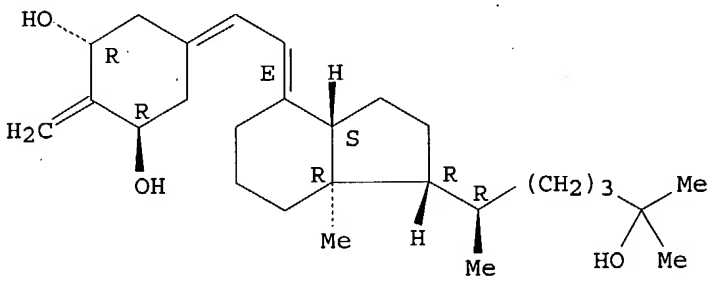
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **213250-70-5P 213319-29-0P**
(preparation of 2-alkylnor-vitamin D compds. and their biol. activities)
RN 213250-70-5 USPATFULL
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 213319-29-0 USPATFULL
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



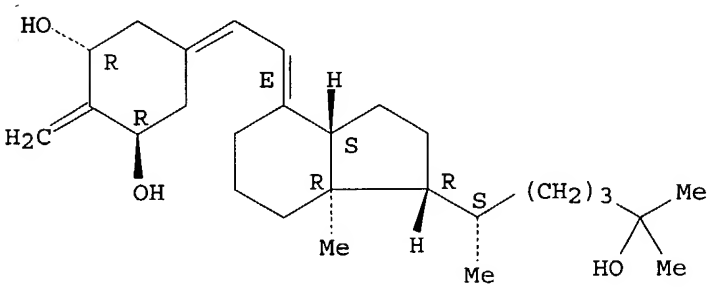
L33 ANSWER 7 OF 22 USPATFULL on STN
AN 2002:228475 USPATFULL
TI 26,27-homologated-20-epi-2-alkyl-19-nor-vitamin D compounds
IN DeLuca, Hector F., Deerfield, WI, UNITED STATES
Sicinski, Rafal R., Warsaw, POLAND
PA Wisconsin Alumni Research Foundation, Madison, WI, UNITED STATES (U.S. corporation)
PI US 2002123638 A1 20020905
US 6544969 B2 20030408
AI US 2001-999299 A1 20011031 (9)
RLI Division of Ser. No. US 2000-541470, filed on 31 Mar 2000, PATENTED Continuation-in-part of Ser. No. US 1999-454013, filed on 3 Dec 1999, PATENTED Division of Ser. No. US 1998-135463, filed on 17 Aug 1998, PATENTED Continuation-in-part of Ser. No. US 1997-819694, filed on 17 Mar 1997, PATENTED
DT Utility
FS APPLICATION
LREP Thomas M. Wozny, ANDRUS, SCEALES, STARKE & SAWALL, LLP, Suite 1100, 100 East Wisconsin Avenue, Milwaukee, WI, 53202-4178
CLMN Number of Claims: 46
ECL Exemplary Claim: 1
DRWN 6 Drawing Page(s)
LN.CNT 2103
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides a novel class of vitamin D related compounds, namely, the 2-alkyl-19-nor-vitamin D derivatives, as well as a general method for their chemical synthesis. The compounds have the formula: ##STR1##

where Y.sub.1 and Y.sub.2, which may be the same or different, are each

selected from the group consisting of hydrogen and a hydroxy-protecting group, R.sub.6 is selected from the group consisting of alkyl, hydroxyalkyl and fluoroalkyl, and where the group R represents any of the typical side chains known for vitamin D type compounds. These 2-substituted compounds, especially the 2α-methyl and the 2α-methyl-20S derivatives, are characterized by relatively high intestinal calcium transport activity and relatively high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. These compounds also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis.

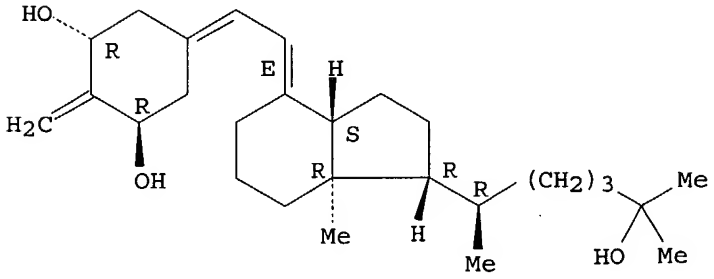
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **213250-70-5P 213319-29-0P**
(preparation of 2-alkylnor-vitamin D compds. and their biol. activities)
RN 213250-70-5 USPATFULL
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 213319-29-0 USPATFULL
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



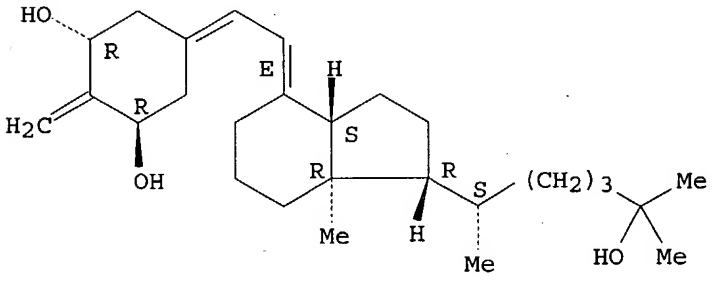
L33 ANSWER 8 OF 22 USPATFULL on STN
AN 2002:165381 USPATFULL
TI 26,27-homologated-20-EPI-2-alklidene-19-nor-vitamin D compounds
IN DeLuca, Hector F., Deerfield, WI, UNITED STATES
Sicinski, Rafal R., Warsaw, POLAND
PA Wisconsin Alumni Research Foundation of Madison (U.S. corporation)
PI US 2002087015 A1 20020704

PI US 6537981 B2 20030325
AI US 2001-1711 A1 20011031 (10)
RLI Division of Ser. No. US 2000-540686, filed on 31 Mar 2000, PENDING
Continuation of Ser. No. US 1998-151113, filed on 10 Sep 1998, PATENTED
Division of Ser. No. US 1997-819693, filed on 17 Mar 1997, PATENTED
DT Utility
FS APPLICATION
LREP Thomas M. Wozny, ANDRUS, SCEALES, STARKE & SAWALL, LLP, Suite 1100, 100 East Wisconsin Avenue, Milwaukee, WI, 53202-4178
CLMN Number of Claims: 48
ECL Exemplary Claim: 1
DRWN 2 Drawing Page(s)
LN.CNT 1601
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides a novel class of vitamin D related compounds, namely, the 2-alkylidene-19-nor-vitamin D derivatives, as well as a general method for their chemical synthesis. The compounds have the formula: ##STR1##

where Y.sub.1 and Y.sub.2, which may be the same or different, are each selected from the group consisting of hydrogen and a hydroxy-protecting group, R.sub.6 and R.sub.8, which may be the same or different, are each selected from hydrogen, alkyl, hydroxyalkyl and fluoroallly, or when taken together represent the group --(CH.sub.2).sub.X-- where x is an integer from 2 to 5, and where the group R represents any of the typical side chains known for vitamin D type compounds. These 2-substituted compounds are characterized by relatively high intestinal calcium transport activity and relatively high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. These compounds also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **213250-70-5P**
(preparation of 2-alkylidenenor-vitamin D compds.)
RN 213250-70-5 USPATFULL
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



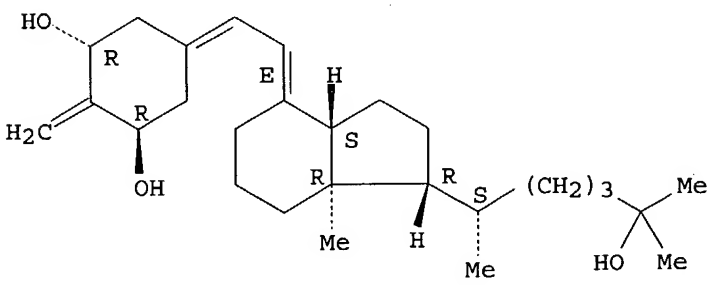
L33 ANSWER 9 OF 22 USPATFULL on STN
AN 2002:116429 USPATFULL
TI 26,27-homologated-20-EPI-2-alkylidene-19-nor-vitamin D compounds
IN DeLuca, Hector F., Deerfield, WI, United States
Sicinski, Rafal R., Warsaw, POLAND

PA Wisconsin Alumni: Research Foundation, Madison, WI, United States (U.S. corporation)
PI US 6392071 B1 20020521
AI US 2000-540686 20000331 (9)
RLI Continuation-in-part of Ser. No. US 1999-370966, filed on 10 Aug 1999, now abandoned Continuation of Ser. No. US 1998-151113, filed on 10 Sep 1998, now patented, Pat. No. US 5936133 Division of Ser. No. US 1997-819693, filed on 17 Mar 1997, now patented, Pat. No. US 5843928
DT Utility
FS GRANTED
EXNAM Primary Examiner: Qazi, Sabiha
LREP Andrus, Sceales, Starke & Sawall, LLP
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 1372
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides a novel class of vitamin D related compounds, namely, the 2-alkylidene-19-nor-vitamin D derivatives, as well as a general method for their chemical synthesis. The compounds have the formula: ##STR1##

where Y.sub.1 and Y.sub.2, which may be the same or different, are each selected from the group consisting of hydrogen and a hydroxy-protecting group, R.sub.6 and R.sub.8, which may be the same or different, are each selected from hydrogen, alkyl, hydroxyalkyl and fluoroalkyl, or when taken together represent the group --(CH.sub.2).sub.x-- where x is an integer from 2 to 5, and where the group R represents any of the typical side chains known for vitamin D type compounds. These 2-substituted compounds are characterized by relatively high intestinal calcium transport activity and relatively high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. These compounds also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **213250-70-5P 213319-29-0P**
(preparation of 26,27-homologated-20-epi-2-alkylidene-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)
RN 213250-70-5 USPATFULL
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

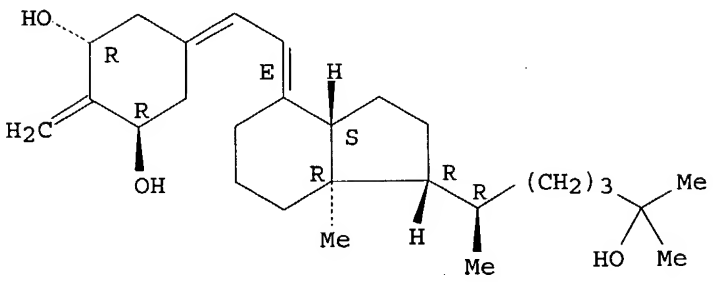
Absolute stereochemistry.
Double bond geometry as shown.



RN 213319-29-0 USPATFULL
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,

(1α,3β,7E)- (9CI) (CA INDEX NAME)

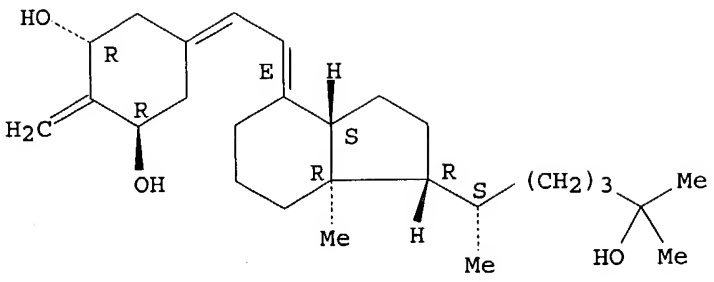
Absolute stereochemistry.
Double bond geometry as shown.



L33 ANSWER 10 OF 22 USPATFULL on STN
AN 2002:99449 USPATFULL
TI 1alpha-hydroxy-2-methylene-19-nor-homopregnacalciferol and its uses
IN DeLuca, Hector F., Deerfield, WI, UNITED STATES
Sicinski, Rafal R., Warsaw, POLAND
Gowlugari, Sumithra, Madison, WI, UNITED STATES
Plum, Lori A., Madison, WI, UNITED STATES
Clagett-Dame, Margaret, Deerfield, WI, UNITED STATES
PI US 2002052350 A1 20020502
US 6440953 B2 20020827
AI US 2001-878438 A1 20010611 (9)
RLI Continuation-in-part of Ser. No. US 2000-657828, filed on 8 Sep 2000, PENDING
DT Utility
FS APPLICATION
LREP Thomas M. Wozny, ANDRUS, SCEALES, STARKE & SAWALL, LLP, 100 East Wisconsin Avenue, Suite 1100, Milwaukee, WI, 53202-4178
CLMN Number of Claims: 33
ECL Exemplary Claim: 1
DRWN 7 Drawing Page(s)
LN.CNT 502
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention discloses 1α-hydroxy-2-methylene-19-nor-homopregnacalciferol and pharmaceutical uses therefor. This compound exhibits pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. This compound also has little, if any, calcemic activity and therefore may be used to treat immune disorders in humans as well as renal osteodystrophy.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **213250-70-5**
(hydroxymethylenenorhomopregnacalciferol and therapeutic use)
RN 213250-70-5 USPATFULL
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

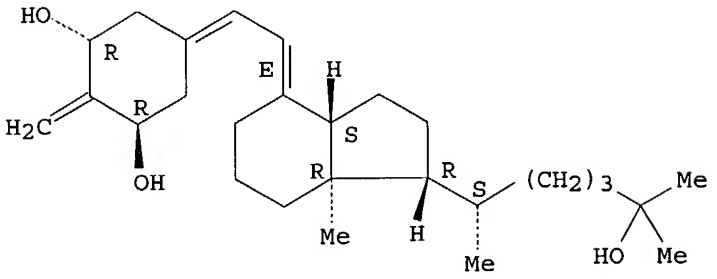


L33 ANSWER 11 OF 22 USPATFULL on STN
AN 2001:202815 USPATFULL
TI 26,27-Homologated-20-EPI-2alkyl-19-nor-vitamin D compounds
IN DeLuca, Hector F., Deerfield, WI, United States
Sicinski, Rafal R., Warsaw, Poland
PA Wisconsin Alumni Research Foundation, Madison, WI, United States (U.S. corporation)
PI US 6316642 B1 20011113
AI US 2000-541470 20000331 (9)
RLI Continuation-in-part of Ser. No. US 1999-454013, filed on 3 Dec 1999 Division of Ser. No. US 1998-135463, filed on 17 Aug 1998, now patented, Pat. No. US 6127559 Continuation-in-part of Ser. No. US 1997-819694, filed on 17 Mar 1997, now patented, Pat. No. US 5945410
DT Utility
FS GRANTED
EXNAM Primary Examiner: Qazi, Sabiha
LREP Andrus, Sceales, Starke & Sawall, LLP
CLMN Number of Claims: 13
ECL Exemplary Claim: 1
DRWN 6 Drawing Figure(s); 6 Drawing Page(s)
LN.CNT 1931
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides a novel class of vitamin D related compounds, namely, 2-alkyl-19-nor-vitamin D derivatives, as well as a general method for their chemical synthesis. The compounds have the formula: ##STR1##

where Y.sub.1 and Y.sub.2, which may be the same or different, are each selected from the group consisting of hydrogen and a hydroxy-protecting group, R.sub.6 is selected from the group consisting of alkyl, hydroxyalkyl and fluoroalkyl, and where the group R represents any of the typical side chains known for vitamin D type compounds. These 2-substituted compounds, especially the 2α-methyl and the 2α-methyl-20S derivatives, are characterized by relatively high intestinal calcium transport activity and relatively high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. These compounds also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis.

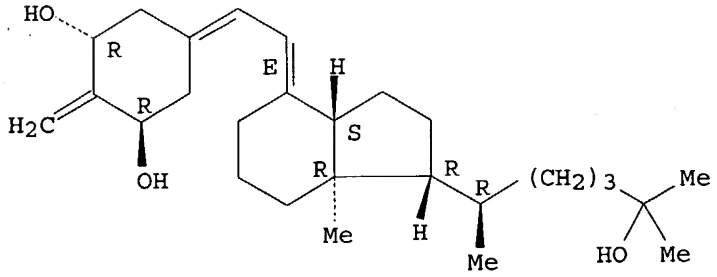
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **213250-70-5P 213319-29-0P**
(preparation of 26,27-homologated-20-epi-2-alkyl-19-norvitamin D compds. with high intestinal calcium transport activity)
RN 213250-70-5 USPATFULL
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 213319-29-0 USPATFULL
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



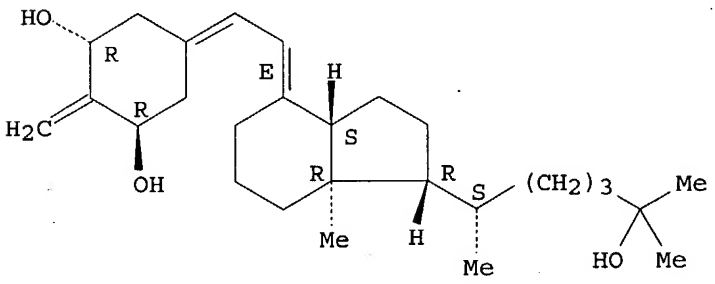
L33 ANSWER 12 OF 22 USPATFULL on STN
AN 2001:136640 USPATFULL
TI 2-alkyl-19-nor-vitamin D compounds
IN DeLuca, Jr., Hector F., Deerfield, WI, United States
Sicinski, Rafal R., Warsaw, Poland
PA Wisconsin Alumni Research Foundation, Madison, WI, United States (U.S. corporation)
PI US 6277837 B1 20010821
AI US 1999-454013 19991203 (9)
RLI Division of Ser. No. US 1998-135463, filed on 17 Aug 1998, now patented, Pat. No. US 6127559 Continuation-in-part of Ser. No. US 1997-819694, filed on 17 Mar 1997, now patented, Pat. No. US 5945410
DT Utility
FS GRANTED
EXNAM Primary Examiner: Qazi, Sabiha
LREP Andrus, Sceales, Starke & Sawall, LLP
CLMN Number of Claims: 23
ECL Exemplary Claim: 1
DRWN 6 Drawing Figure(s); 6 Drawing Page(s)
LN.CNT 1544
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides a novel class of vitamin D related compounds, namely, the 2-alkyl-19-nor-vitamin D derivatives, as well as a general method for their chemical synthesis. The compounds have the formula: ##STR1##

where Y.sub.1 and Y.sub.2, which may be the same or different, are each

selected from the group consisting of hydrogen and a hydroxy-protecting group, R.sub.6 is selected from the group consisting of alkyl, hydroxyalkyl and fluoroalkyl, and where the group R represents any of the typical side chains known for vitamin D type compounds. These 2-substituted compounds, especially the 2α-methyl and the 2α-methyl-20S derivatives, are characterized by relatively low intestinal calcium transport activity and high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. These compounds also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis.

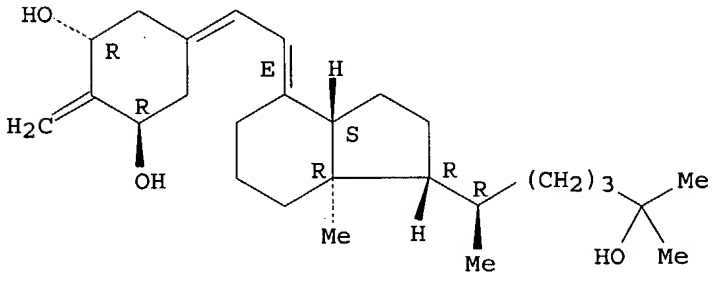
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **213250-70-5P 213319-29-0P**
(preparation of 2-alkylnor-vitamin D compds. and their biol. activities)
RN 213250-70-5 USPATFULL
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 213319-29-0 USPATFULL
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

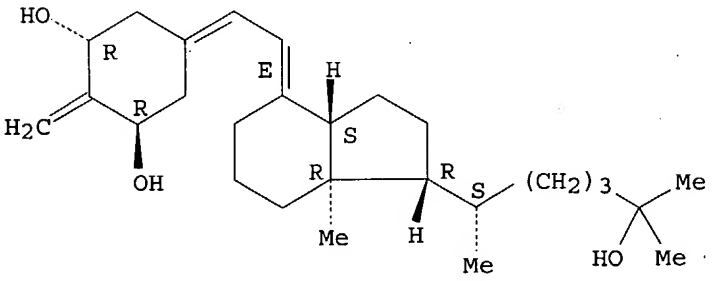


L33 ANSWER 13 OF 22 USPATFULL on STN
AN 2000:132031 USPATFULL
TI 2-alkyl-19-nor-vitamin D compounds
IN DeLuca, Hector F., Deerfield, WI, United States
Sicinski, Rafal R., Warsaw, Poland
PA Wisconsin Alumni Research Foundation, Madison, WI, United States (U.S. corporation)

PI US 6127559 20001003
AI US 1998-135463 19980817 (9)
RLI Continuation-in-part of Ser. No. US 1997-819694, filed on 17 Mar 1997, now patented, Pat. No. US 5945410
DT Utility
FS Granted
EXNAM Primary Examiner: Dees, Jose' G.; Assistant Examiner: Qazi, Sabiha N.
LREP Andrus, Sceales, Starke & Sawall
CLMN Number of Claims: 43
ECL Exemplary Claim: 1
DRWN 6 Drawing Figure(s); 6 Drawing Page(s)
LN.CNT 1575
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides a novel class of vitamin D related compounds, namely, the 2-alkyl-19-nor-vitamin D derivatives, as well as a general method for their chemical synthesis. The compounds have the formula: ##STR1## where Y.sub.1 and Y.sub.2, which may be the same or different, are each selected from the group consisting of hydrogen and a hydroxy-protecting group, R.sub.6 is selected from the group consisting of alkyl, hydroxyalkyl and fluoroalkyl, and where the group R represents any of the typical side chains known for vitamin D type compounds. These 2-substituted compounds, especially the 2α-methyl and the 2α-methyl-20S derivatives, are characterized by relatively low intestinal calcium transport activity and high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. These compounds also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis.

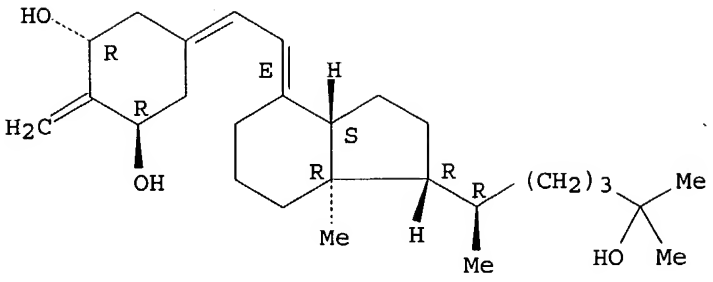
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **213250-70-5P**
(preparation and therapeutic use of 2-alkyl-19-nor-vitamin D analog)
RN 213250-70-5 USPATFULL
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



IT **213319-29-0P**
(preparation and therapeutic use of 2-alkyl-19-nor-vitamin D analog)
RN 213319-29-0 USPATFULL
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

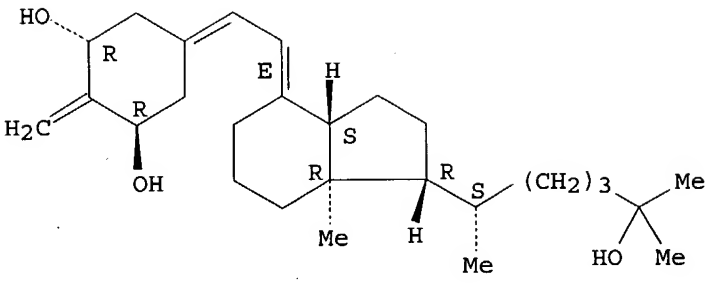
Absolute stereochemistry.
Double bond geometry as shown.



L33 ANSWER 14 OF 22 USPATFULL on STN
AN 1999:102799 USPATFULL
TI 2-alkyl-19-nor-vitamin D compounds
IN DeLuca, Hector F., Deerfield, WI, United States
Rafal, Sicinski R., Warsaw, Poland
PA Wisconsin Alumni Research Foundation, Madison, WI, United States (U.S. corporation)
PI US 5945410 19990831
AI US 1997-819694 19970317 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Dees, Jose' G.; Assistant Examiner: Pryor, Alton
LREP Andrus, Sceales, Starke & Sawall
CLMN Number of Claims: 41
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 1227
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides a novel class of vitamin D related compounds, namely, the 2-alkyl-19-nor-vitamin D derivatives, as well as a general method for their chemical synthesis. The compounds have the formula: ##STR1## where Y.sub.1 and Y.sub.2, which may be the same or different, are each selected from the group consisting of hydrogen and a hydroxy-protecting group, R.sub.6 is selected from the group consisting of alkyl, hydroxyalkyl and fluoroalkyl, and where the group R represents any of the typical side chains known for vitamin D type compounds. These 2-substituted compounds are characterized by low intestinal calcium transport activity and high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. These compounds also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis.

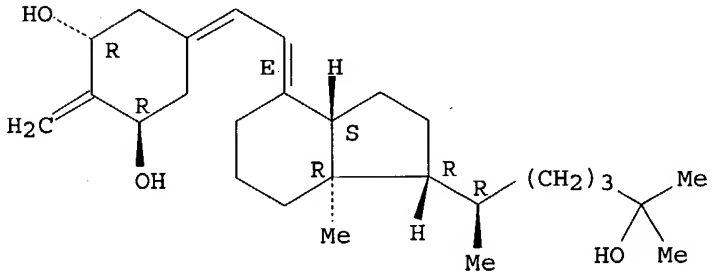
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **213250-70-5P 213319-29-0P**
(preparation of 2-alkylnor-vitamin D compds. and their biol. activities)
RN 213250-70-5 USPATFULL
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 213319-29-0 USPATFULL
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

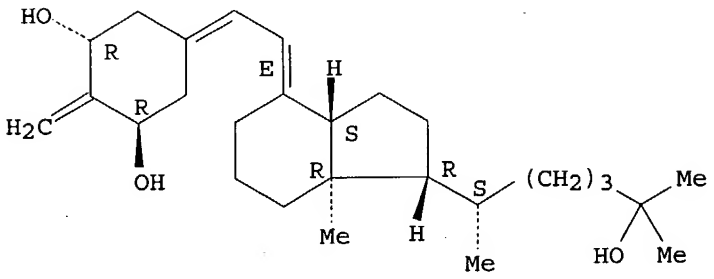


L33 ANSWER 15 OF 22 USPATFULL on STN
AN 1999:92846 USPATFULL
TI 2-alkylidene-19-nor-vitamin D compounds
IN Deluca, Hector F., Deerfield, WI, United States
Sicinski, Rafal R., Warsaw, Poland
PA Wisconsin Alumni Research Foundation, Madison, WI, United States (U.S. corporation)
PI US 5936133 19990810
AI US 1998-151113 19980910 (9)
RLI Division of Ser. No. US 1997-819693, filed on 17 Mar 1997, now patented, Pat. No. US 5843928
DT Utility
FS Granted
EXNAM Primary Examiner: Lambkin, Deborah C.
LREP Andrus, Sceales, Starke & Sawall
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 1051
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides a novel class of vitamin D related compounds, namely, the 2-alkylidene-19-nor-vitamin D derivatives, as well as a general method for their chemical synthesis. The compounds have the formula: ##STR1## where Y.sub.1 and Y.sub.2, which may be the same or different, are each selected from the group consisting of hydrogen and a hydroxy-protecting group, R.sub.6 and R.sub.8, which may be the same or different, are each selected from hydrogen, alkyl, hydroxyalkyl and fluoroalkyl, or when taken together represent the group --(CH.sub.2).sub.x -- where x is an integer from 2 to 5, and where the group R represents any of the typical side chains known for vitamin D

type compounds. These 2-substituted compounds are characterized by low intestinal calcium transport activity and high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. These compounds also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **213250-70-5P**
(preparation of 2-alkylidenenor-vitamin D compds.)
RN 213250-70-5 USPATFULL
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

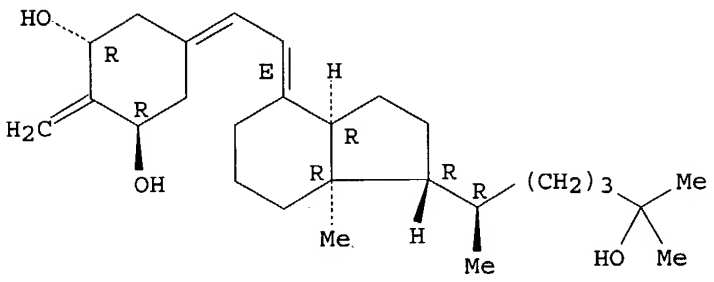


L33 ANSWER 16 OF 22 USPATFULL on STN
AN 1999:92818 USPATFULL
TI 14-EPI-19-nor-vitamin D compounds and methods
IN Paaren, Herbert E., Madison, WI, United States
PA Tetrionics, Inc., Madison, WI, United States (U.S. corporation)
PI US 5936105 19990810
AI US 1998-96330 19980611 (9)
PRAI US 1997-53088P 19970613 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Clardy, S. Mark; Assistant Examiner: Pryor, Alton
LREP Ryndak & Lyerla
CLMN Number of Claims: 1
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 919
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB 19-nor-vitamin D analog compounds and a method of synthesizing such compounds are disclosed. More particularly, examples of such compounds include 14-epi-19-nor-1α,25-dihydroxyvitamin D.sub.3, 14-epi-20-epi-19-nor-1α, 25-dihydroxyvitamin D.sub.3, 14-epi-20-epi-19-nor-1α-hydroxyvitamin D.sub.3, 14-epi-19-nor-1α, 25-dihydroxyvitamin D.sub.2, 14-epi-19-nor-24-homo-1α, 25-didydroxyvitamin D.sub.3, 14-epi-19-nor-20(S)-hydroxymethyl-1α-hydropregnacalciferol, and 14-epi-19-nor-20(R)-hydroxymethyl-1α-hydroxypregnacalciferol.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **235108-14-2P**
(preparation of 14-epi-19-nor-vitamin D compds. with cell differentiation activity)

RN 235108-14-2 USPATFULL
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,14β)- (9CI) (CA INDEX NAME)

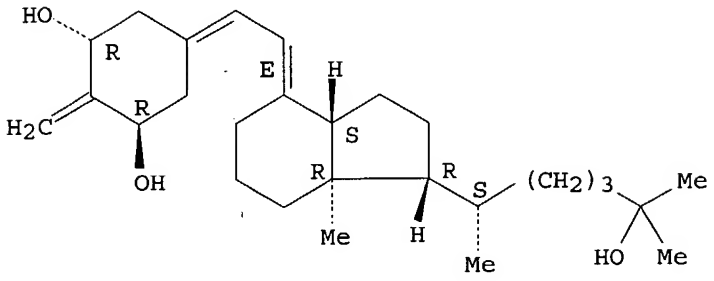
Absolute stereochemistry.
Double bond geometry as shown.



L33 ANSWER 17 OF 22 USPATFULL on STN
AN 1998:150930 USPATFULL
TI 2-alkylidene-19-nor-vitamin D compounds
IN Deluca, Hector F., Deerfield, WI, United States
Rafal, Sicinski R., Warsaw, Poland
PA Wisconsin Alumni Research Foundation, Madison, WI, United States (U.S. corporation)
PI US 5843928 19981201
AI US 1997-819693 19970317 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Lambkin, Deborah C.
LREP Andrus, Sceales, Starke & Sawall
CLMN Number of Claims: 33
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 1153
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides a novel class of vitamin D related compounds, namely, the 2-alkylidene-19-nor-vitamin D derivatives, as well as a general method for their chemical synthesis. The compounds have the formula: ##STR1## where Y.sub.1 and Y.sub.2, which may be the same or different, are each selected from the group consisting of hydrogen and a hydroxy-protecting group, R.sub.6 and R.sub.8, which may be the same or different, are each selected from hydrogen, alkyl, hydroxyalkyl and fluoroalkyl, or when taken together represent the group --(CH.sub.2).sub.x -- where x is an integer from 2 to 5, and where the group R represents any of the typical side chains known for vitamin D type compounds. These 2-substituted compounds are characterized by low intestinal calcium transport activity and high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. These compounds also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **213250-70-5P**
(preparation of 2-alkylidenenor-vitamin D compds.)
RN 213250-70-5 USPATFULL
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

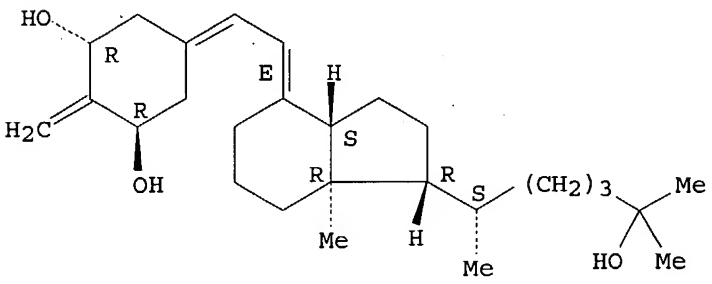


L33 ANSWER 18 OF 22 USPAT2 on STN
AN 2003:258374 USPAT2
TI 26,27-homologated-20-EPI-2-alkylidene-19-nor-vitamin D compounds
IN DeLuca, Hector F., Deerfield, WI, United States
Sicinski, Rafal R., Warsaw, POLAND
PA Wisconsin Alumni Research Foundation, Madison, WI, United States (U.S. corporation)
PI US 6696431 B2 20040224
AI US 2003-352745 20030128 (10)
RLI Division of Ser. No. US 2001-1711, filed on 31 Oct 2001, now patented, Pat. No. US 6537981 Division of Ser. No. US 2000-540686, filed on 31 Mar 2000, now patented, Pat. No. US 6392071 Continuation of Ser. No. US 1999-370966, filed on 10 Aug 1999, now abandoned Continuation of Ser. No. US 1998-151113, filed on 10 Sep 1998, now patented, Pat. No. US 5936133 Division of Ser. No. US 1997-819693, filed on 17 Mar 1997, now patented, Pat. No. US 5843928
DT Utility
FS GRANTED
EXNAM Primary Examiner: Qazi, Sabiha
LREP Andrus, Sceales, Starke & Sawall, LLP
CLMN Number of Claims: 2
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 1382
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides a novel class of vitamin D related compounds, namely, the 2-alkylidene-19-nor-vitamin D derivatives, as well as a general method for their chemical synthesis. The compounds have the formula: ##STR1##

where Y.sub.1 and Y.sub.2, which may be the same or different, are each selected from the group consisting of hydrogen and a hydroxy-protecting group, R.sub.6 and R.sub.8, which may be the same or different, are each selected from hydrogen, alkyl, hydroxyalkyl and fluoroalkyl, or when taken together represent the group --(CH.sub.2).sub.x-- where x is an integer from 2 to 5, and where the group R represents any of the typical side chains known for vitamin D type compounds. These 2-substituted compounds are characterized by relatively high intestinal calcium transport activity and relatively high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. These compounds also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **213250-70-5P**
(preparation of 2-alkylidenenor-vitamin D compds.)
RN 213250-70-5 USPAT2
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



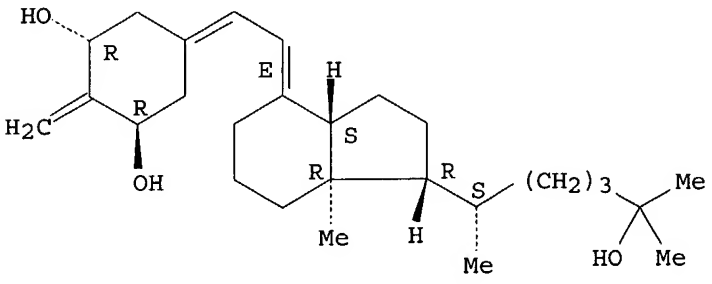
L33 ANSWER 19 OF 22 USPAT2 on STN
AN 2003:106944 USPAT2
TI 26,27-Homologated-20-EPI-2-alkyl-19-NOR-vitamin D compounds
IN DeLuca, Hector F., Deerfield, WI, United States
Sicinski, Rafal R., Warsaw, POLAND
PA Wisconsin Alumni Research Foundation, Madison, WI, United States (U.S. corporation)
PI US 6667298 B2 20031223
AI US 2002-246968 20020919 (10)
RLI Division of Ser. No. US 2001-999299, filed on 31 Oct 2001, now patented, Pat. No. US 6544969, issued on 4 Aug 2000 Division of Ser. No. US 2000-541470, filed on 31 Mar 2000, now patented, Pat. No. US 6316642 Continuation-in-part of Ser. No. US 1999-454013, filed on 3 Dec 1999, now patented, Pat. No. US 6277837 Division of Ser. No. US 1998-135463, filed on 17 Aug 1998, now patented, Pat. No. US 6127559 Continuation-in-part of Ser. No. US 1997-819694, filed on 17 Mar 1997, now patented, Pat. No. US 5945410
DT Utility
FS GRANTED
EXNAM Primary Examiner: Qazi, Sabiha
LREP Andrus, Sceales, Starke & Sawall, LLP
CLMN Number of Claims: 20
ECL Exemplary Claim: 1
DRWN 6 Drawing Figure(s); 6 Drawing Page(s)
LN.CNT 1913
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides a novel class of vitamin D related compounds, namely, the 2-alkyl-19-nor-vitamin D derivatives, as well as a general method for their chemical synthesis. The compounds have the formula: ##STR1##

where Y.sub.1 and Y.sub.2, which may be the same or different, are each selected from the group consisting of hydrogen and a hydroxy-protecting group, R.sub.6 is selected from the group consisting of alkyl, hydroxyalkyl and fluoroalkyl, and where the group R represents any of the typical side chains known for vitamin D type compounds. These 2-substituted compounds, especially the 2α-methyl and the 2α-methyl-20S derivatives, are characterized by relatively high intestinal calcium transport activity and relatively high bone calcium mobilization activity resulting in novel therapeutic agents for the

treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. These compounds also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis.

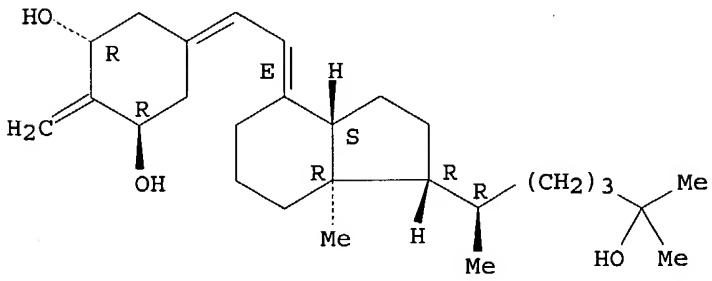
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **213250-70-5P 213319-29-0P**
(preparation of 2-alkylnor-vitamin D compds. and their biol. activities)
RN 213250-70-5 USPAT2
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 213319-29-0 USPAT2
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



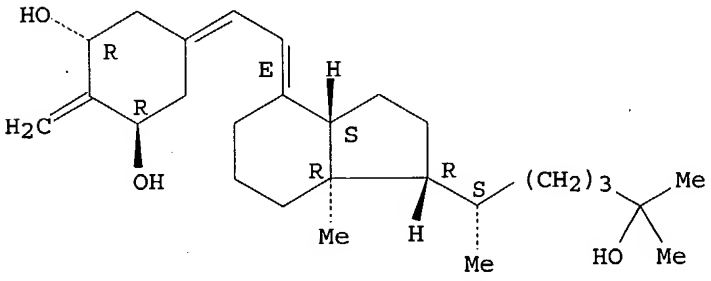
L33 ANSWER 20 OF 22 USPAT2 on STN
AN 2002:228475 USPAT2
TI 26,27-homologated-20-epi-2-alkyl-19-nor-vitamin D compounds
IN DeLuca, Hector F., Deerfield, WI, United States
Sicinski, Rafal R., Warsaw, POLAND
PA Wisconsin Alumni Research Foundation, Madison, WI, United States (U.S. corporation)
PI US 6544969 B2 20030408
AI US 2001-999299 20011031 (9)
RLI Division of Ser. No. US 2000-541470, filed on 31 Mar 2000, now patented, Pat. No. US 6316642 Continuation-in-part of Ser. No. US 1999-454013, filed on 3 Dec 1999, now patented, Pat. No. US 6277837 Division of Ser. No. US 1998-135463, filed on 17 Aug 1998, now patented, Pat. No. US 6127559 Continuation-in-part of Ser. No. US 1997-819694, filed on 17 Mar 1997, now patented, Pat. No. US 5945410

DT Utility
FS GRANTED
EXNAM Primary Examiner: Qazi, Sabiha
LREP Andrus, Sceales, Starke & Sawall, LLP
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN 6 Drawing Figure(s); 6 Drawing Page(s)
LN.CNT 1884
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides a novel class of vitamin D related compounds, namely, the 2-alkyl-19-nor-vitamin D derivatives, as well as a general method for their chemical synthesis. The compounds have the formula: ##STR1##

where Y.sub.1 and Y.sub.2, which may be the same or different, are each selected from the group consisting of hydrogen and a hydroxy-protecting group, R.sub.6 is selected from the group consisting of alkyl, hydroxyalkyl and fluoroalkyl, and where the group R represents any of the typical side chains known for vitamin D type compounds. These 2-substituted compounds, especially the 2α-methyl and the 2α-methyl-20S derivatives, are characterized by relatively high intestinal calcium transport activity and relatively high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. These compounds also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis.

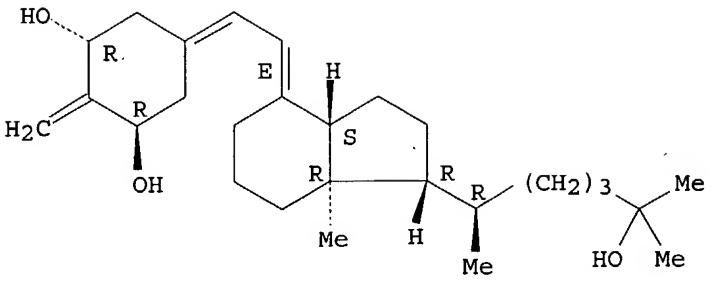
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **213250-70-5P 213319-29-0P**
(preparation of 2-alkylnor-vitamin D compds. and their biol. activities)
RN 213250-70-5 USPAT2
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 213319-29-0 USPAT2
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

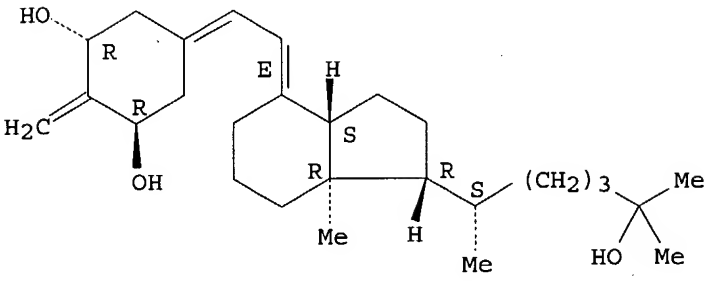


L33 ANSWER 21 OF 22 USPAT2 on STN
AN 2002:165381 USPAT2
TI 26,27-Homologated-20-EPI-2-alklidene-19-nor-vitamin D compounds
IN DeLuca, Hector F., Deerfield, WI, United States
Sicinski, Rafal R., Warsaw, POLAND
PA Wisconsin Alumni Research Foundation, Madison, WI, United States (U.S. corporation)
PI US 6537981 B2 20030325
AI US 2001-1711 20011031 (10)
RLI Division of Ser. No. US 2000-540686, filed on 31 Mar 2000 Continuation of Ser. No. US 1998-151113, filed on 10 Sep 1998, now patented, Pat. No. US 5936133 Division of Ser. No. US 1997-819693, filed on 17 Mar 1997, now patented, Pat. No. US 5843928
DT Utility
FS GRANTED
EXNAM Primary Examiner: Qazi, Sabiha
LREP Andrus, Sceales, Starke & Sawall, LLP
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 1385
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides a novel class of vitamin D related compounds, namely, the 2-alkylidene-19-nor-vitamin D derivatives, as well as a general method for their chemical synthesis. The compounds have the formula: ##STR1##

where Y.sub.1 and Y.sub.2, which may be the same or different, are each selected from the group consisting of hydrogen and a hydroxy-protecting group, R.sub.6 and R.sub.8, which may be the same or different, are each selected from hydrogen, alkyl, hydroxyalkyl and fluoroallly, or when taken together represent the group --(CH.sub.2).sub.X-- where x is an integer from 2 to 5, and where the group R represents any of the typical side chains known for vitamin D type compounds. These 2-substituted compounds are characterized by relatively high intestinal calcium transport activity and relatively high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. These compounds also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **213250-70-5P**
(preparation of 2-alkylidenenor-vitamin D compds.)
RN 213250-70-5 USPAT2
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

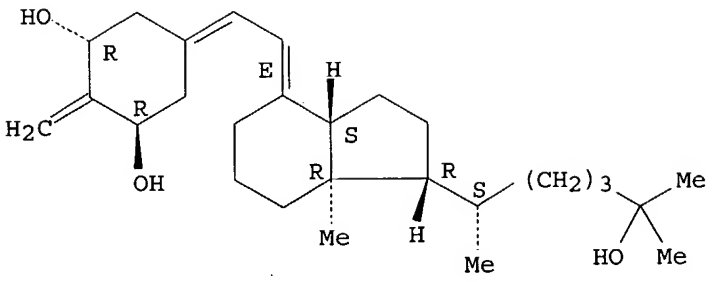
Absolute stereochemistry.
Double bond geometry as shown.



L33 ANSWER 22 OF 22 USPAT2 on STN
AN 2002:99449 USPAT2
TI 1α-hydroxy-2-methylene-19-nor-homopregnacalciferol and its uses
IN DeLuca, Hector F., Deerfield, WI, United States
Sicinski, Rafal R., Warsaw, POLAND
Gowlugari, Sumithra, Madison, WI, United States
Plum, Lori A., Madison, WI, United States
Clagett-Dame, Margaret, Deerfield, WI, United States
PA Wisconsin Alumni Research Foundation, Madison, WI, United States (U.S. corporation)
PI US 6440953 B2 20020827
AI US 2001-878438 20010611 (9)
RLI Continuation-in-part of Ser. No. US 2000-657828, filed on 8 Sep 2000
DT Utility
FS GRANTED
EXNAM Primary Examiner: Qazi, Sabiha
LREP Andrus, Sceales, Starke & Sawall, LLP
CLMN Number of Claims: 26
ECL Exemplary Claim: 1
DRWN 7 Drawing Figure(s); 7 Drawing Page(s)
LN.CNT 485
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention discloses 1α-hydroxy-2-methylene-19-nor-homopregnacalciferol and pharmaceutical uses therefor. This compound exhibits pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anticancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. This compound also has little, if any, calcemic activity and therefore may be used to treat immune disorders in humans as well as renal osteodystrophy.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **213250-70-5**
(hydroxymethylenenorhomopregnacalciferol and therapeutic use)
RN 213250-70-5 USPAT2
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

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               E CLAGETTE M/AU
L2            1 S E2
               E CLAGETTE D/AU
               E DAME M/AU
L3           12 S E3,E4,E6-E8
               E DELUCA H/AU
L4         1160 S E3,E6-E10
               E DE LUCA H/AU
L5           38 S E5,E6
L6         1213 S L1-L5

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L10         294 S L9 AND 3/O
L11          92 S L10 AND 27/C
L12          54 S L11 AND 44/H
L13          23 S L12 AND 1 3 25 TRIOL
L14           2 S L13 AND 2 METHYLENE
L15          52 S L12 NOT L14
L16             STR
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L18           3 S L16 FAM FUL
               SAV L18 QAZI782/A
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L23           3 S L21 NOT L22
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L24           22 S L21-L23
L25            0 S L24 AND LIFE(L)EXPECT?
L26            0 S L24 AND LONGEV?
                 E LONGEVITY/CT
                 E E3+ALL
L27            1 S L24 AND E3+OLD,NT,PFT,RT
L28           22 S L24,L27

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     FILE 'HCAPLUS' ENTERED AT 13:50:36 ON 05 SEP 2004
L30           21 S L28 NOT L27

     FILE 'USPATFULL, USPAT2' ENTERED AT 13:51:17 ON 05 SEP 2004
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L32            2 S L29 AND (AGING? OR AGEING? OR LONGEV?)/CT,BI
L33           22 S L29 NOT L32

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